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(54) Title: ALGORITHMIC DETERMINATION OF FLANKING DNA SEQUENCES THAT CONTROL THE EXPRESSION OF SETS OF GENES IN PROKARYOTIC, ARCHEA AND EUKARYOTIC GENOMES

(57) Abstract: An algorithm has been developed to identify four DNA sequences of 20 bases or more that form a structure called a connectron. Two sequences C1 and C2 are adjacent to each other. These sequences are expressed as RNA in the 3'UTR of some genes in many prokaryotic, archea and eukaryotic genomes. The other half of a connectron is two DNA sequences T1 and T2 that are on the same chromosome and range in distance from each other by about 1kb to 105kb. The C1 sequence is identical to the T1 sequence and the C2 sequence is identical to the T2 sequence. C1/C2 and T1-T2 can be on different chromosomes. The C1/C2 RNA sequence of the gene transcript finds the two double-stranded DNA sequences T1 and T2. The single-stranded RNA and double-stranded DNA then form a triple-stranded Hoogsteen helix of the RNA/DNA/DNA variety. Because the C1 sequence is adjacent to the C2 sequence, the T1 sequence is made spatially adjacent to the T2 sequence in a compact X-shaped structure. Chromatin particles form as compact 30nm assemblies in the DNA between T1 and T2 thus eliminating the intervening genes from promotion and expression. Connectrons remove sets of genes from expression and thus modulate the behavior of many types of cells.

**ALGORITHMIC DETERMINATION OF FLANKING DNA SEQUENCES
THAT CONTROL THE EXPRESSION OF SETS OF GENES IN
PROKARYOTIC, ARCHEA AND EUKARYOTIC GENOMES**

5 **Reference to Related Application**

The present application is the subject of Provisional Application Serial No. 60/208,650 filed June 2, 2000 entitled ALGORITHMIC DETERMINATION OF CONNECTRONS FOR THE HIGH LEVEL REGULATION OF GENE EXPRESSION.

10 **Introduction**

RNA introduced into a cell by a virus is now known to trigger a cellular defense mechanism known as post-transcriptional gene silencing (PTGS). If the viral RNA sequence matches a sequence within the cell's genome the associated genes are turned off or silenced. This phenomenon is also called 'RNA interference' or RNAi. A single-stranded RNA can interact with another single-stranded RNA (known as antisense RNA). The single-stranded RNA can also form a triple-stranded complex with double-stranded DNA. This triple-stranded complex is known as a Hoogsteen helix. This patent application shows how two specific adjacent RNA single-stranded sequences (called C1 and C2 – for Control Sequence 1 and Control Sequence 2) interact with two distant double-stranded DNA sequences (called T1 and T2 – for Target Sequence 1 and Target Sequence 2) to form a tetradic relationship which is called a "connectron". The two distant DNA double-stranded sequences (T1 and T2) must be on the same chromosome in a genome and they must be between about 1kb and 105kb of each other. The adjacent single-stranded RNA sequences (C1/C2) can be on the same or different chromosome as the T1 and T2 sequences. The C1 sequence is identical to the T1 sequence and the C2 sequence is identical to the T2

sequence. The connectron acts to stabilize the double-stranded DNA by allowing 30nm chromatin particles to form. Genes that lie between the T1 and T2 sequences when wrapped up in 30nm chromatin particles are not open to promotion and expression. The connectron (i.e. the tetradic relationship between the T1-T2 sequences and C1/C2 sequences) provides a general explanation for PTGS. A connectron can be implemented by RNA sequences, PNA (Peptide Nucleic Acid) sequences or by a zinc-finger DNA Binding Protein (DBP) specific to the T1 and T2 sequences.

Characteristically the adjacent C1/C2 sequences lie in the 3'UTR of a gene. The T1 and T2 sequences do not lie within the translated region of any gene. These sequences "surround" one or more genes. There are, however, T1 and T2 sequence pairs that surround one or more C1/C2 sequences that are not 3'UTR to any gene. These are called "geneless connectrons". There may be promoter sequences that cause the transcription of these 3'UTR sequences.

A computer-based algorithm that is similar to the algorithm used in the US Patent 6,205,404 has been developed to determine the connectron structure of any genome. This algorithm determines the existence of all the connectrons in the genomic DNA. Connectrons exist in prokaryotes, archaea, single-celled eukaryotes, multi-celled eukaryotes, plants and higher animals. Connectron relationships exist between prokaryotes and their plasmids. The geneless connectrons provide a possible mechanism for forming a hierarchy of gene expression control that will produce an understanding of cell differentiation and tissue development.

Each connectron is a unique tetrad of sequences. Each connectron changes the expression of the genes between the T1 and T2 sequences. The C1 sequence (which is equivalent to the T1 sequence) and the C2 sequence (which is equivalent to the T2 sequence) are determined by the invention described in this patent application. In general, the tetrad of connectron sequences can be patented because the structure of matter is known and the function of specific gene expression modulation is also known. Gene expression modification can be produced by introducing antisense

RNA or PNA to interact C1/C2 RNA sequences or zinc-finger DBPs to interact with the T1 and T2 sequences. Using connectrons it will be possible to modify cellular and tissue behavior in a very general manner.

Examples will be given from different genomes to illustrate that the connectron is a perfectly general and universal concept.

10

Definitions

Double stranded DNA – Watson and Crick showed in 1953 that DNA naturally forms a double-stranded helix. A typical double stranded sequence is

15

5'-TAGAGGAGTACCAAC-3'
3'-ATCTCCTCATGGTG-5'

20

Hydrogen Bond - The force between a hydrogen atom and another heavier atom such as Oxygen (O), Nitrogen (N), Phosphorus (P), or Sulfur (S).

Positive strand – The positive strand is normally represented 5' to 3' running left to right as in

25

5'-TAGAGGAGTACCAAC-3'

Negative strand – The negative strand is normally represented 5' to 3' running right to left as in

30

3'-ATCTCCTCATGGTG-5'

Single stranded RNA – Either the positive or the negative strand of the double-stranded DNA can be transcribed by the polymerase. In RNA U replaces T.

5 RNA of positive strand sequence 5'-UAGAGGAGUACCAC-3'
RNA of negative strand sequence 5'-GUGGUACUCCUCUA-3'

Antisense RNA – The antisense strand of any RNA sequence is the compliment sequence

10 RNA sequence 5'-UAGAGGAGUACCAC-3'
Antisense RNA sequence 3'-AUCUCCUCAUGGUG-5'

15 Triple Strand Helix – The RNA sequence of a RNA/DNA triple-strand complex is the same as the positive strand of the DNA

DNA positive strand 5'-TAGAGGAGTACCAAC-3'
DNA negative strand 3'-ATCTCCTCATGGTG-5'
RNA strand 5'-UAGAGGAGUACCAC-3'

20 Promoter – Any region of DNA, that binds proteins which engage the polymerase transcription mechanism.

TATA Box – A region near the 3' end of a promoter with the sequence TATA.

25 mRNA – The RNA produced from the DNA by the polymerase as a result of transcription

30 Start of transcription – The 3' end of a promoter where the polymerase mechanism begins to transcribe DNA into mRNA.

Exon – Any region of mRNA which is used to code for proteins

Intron – Any region of mRNA lying between two exons which is not used to code for proteins. The introns are edited out of the initial RNA transcript to form the mature mRNA.

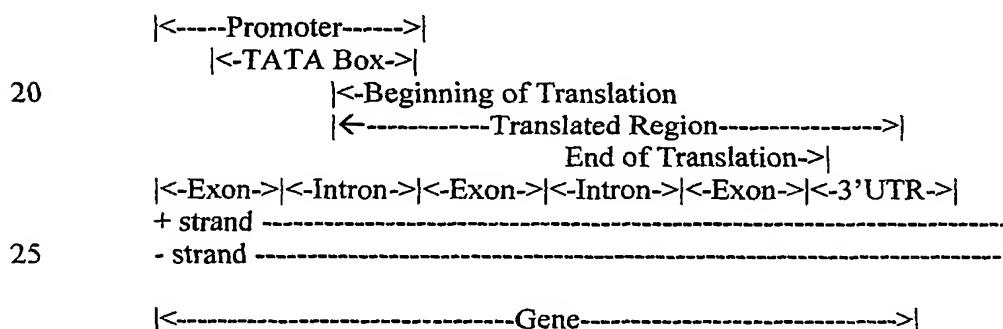
5

3' UTR – The untranslated 3' end of an mRNA is beyond the end of the last exon. A stop codon in the mRNA causes the ribosome to stop the translation of mRNA into protein.

10 End of translation – The 3' end of the 3'-most exon.

Translated region – Any collection of exons and introns.

15 Gene – Any DNA region that codes for a protein. Introns do not occur in prokaryotic genes and they sometime fail to occur in eukaryotic genes. A typical model of a gene is



20 Positive strand gene – Any gene in which the features run 5' to 3' on the positive strand

25 Negative strand gene – Any gene in which the features run 5' to 3' on the negative strand

30 35 C1 sequence – Any positive or negative strand DNA sequence of 20 bases or more.

The C2 sequence must occur in the same chromosome as the C1 sequence.

C2 sequence – Any positive or negative strand DNA sequence of 20 bases or more.

The C1 sequence must occur in the same chromosome as the C2 sequence.

5

C1/C2 – Any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence

T1 sequence – Any positive or negative strand DNA sequence of 20 bases or more

10 that is on the same chromosome as the T2 sequence. The T1 and T2 sequences must be between about 1kb and 105kb apart.

T2 sequence – Any positive or negative strand DNA sequence of 20 bases or more

15 that is on the same chromosome as the T1 sequence. The T2 and T1 sequences must be between about 1kb and 105kb apart.

Last exon gap or Gap-Distance – The number of bases between the end of transcription and the beginning of the C1/C2 sequence. In prokaryotes and single-celled eukaryotes this gap can range from no bases to 500 bases. In multi-celled eukaryotes the gap can be as large as 10,000 bases.

Poly-adenylation signal – A number of Adenosine (A) bases are added to the mRNA at the end of the 3'UTR.

25 Possible Connectron – Any set of T1, T2 and C1/C2 sequences such that the C1 sequence is identical to the T1 sequence and the C2 sequence is identical to the T2 sequence. The promoter of some gene causes the mRNA of the gene to be expressed. The mRNA is edited to eliminate the introns. The whole mRNA including the 3'UTR

30 can move about in the cell or the nucleus of the cell. The C1/C2 RNA that is part of the 3'UTR moves to the T1 and T2 DNA sequences. A triple-stranded complex of the DNA and the RNA forms such that the C1 sequence forms hydrogen bonds with the T1 sequence and the C2 sequence forms hydrogen bonds with the T2 sequence.

Because the C1 sequence is adjacent to the C2 sequence, the T1 sequence is brought physically close to the T2 sequence. This produces a loop of between about 1kb and 105kb in the DNA. Histone proteins reduce the length of the DNA by binding 200 bases. Histone/DNA complexes form six-fold symmetry chromatin assemblies. The diameter of the chromatin assemblies is approximately 30nm.

5

Real Connectron – Any Possible Connectron which is within the Gap-Distance of some gene

10

Homologous connectron – The T1 sequence and the T2 sequence are on the same chromosome as the C1/C2 sequence

Heterologous connectron – The T1 sequence and the T2 sequence are on a chromosome different from chromosome of the C1/C2 sequence

15

Permanent connectron – Any C1/C2 sequence, which is 3' UTR to some gene that is not surrounded by any T1 and T2 sequence pairs

20

Transient connectron – Any C1/C2 sequence, which is 3' UTR to some gene that is surrounded by one or more T1 and T2 sequence pairs

Self-limiting connectron – Any C1/C2 sequence which is 3'UTR to some gene that is surrounded by the T1 and T2 sequences such that C1=T1 and C2=T2

25

Geneless connectron - Any C1/C2 sequence which is not 3'UTR to some gene but is surrounded by some T1 and T2. A promoter may lie 5' to the C1/C2 sequence.

30

Bidirectionality of Connectron Excitation – A C1/C2 short loop on one strand selects a T1-T2 long loop pair on the same or the opposite strand. The C1/C2 short loop has a complementary C1'/C2' sequence on the opposite strand. Similarly the T1-T2 long loop pair has a complementary long loop pair T1'-T2'. Wherever a C1/C2, T1-T2 tetrad exists there is a complementary C1'/C2', T1'-T2' tetrad. The C1/C2 short loop

can be transcribed as a 3'UTR to a gene on the same strand. The C1'/C2' short loop which is on the strand opposite to the C1/C2 short loop can also be transcribed as a 3'UTR to a gene on the same strand. There are four possible models of action

T1 T2 gene - C1/C2

+ strand -----
 - strand -----

5

T1 T2

+ strand -----
 - strand -----

10

C2/C1 - gene

+ strand -----
 - strand -----

15

T2' T1' C2'/C1' - gene

gene - C1'/C2'

+ strand -----
 - strand -----

20

T2' T1'

Of course, the short loops and the long loops do not have to be on the same chromosome.

25

Hierarchy of connectron action – When a C1/C2 is expressed it forms a T1-T2 loop by forming a connectron. The C1/C2 sequence does not have to be on the same chromosome as the T1 and T2 sequences. This provides a way of causing interaction between chromosomes. When the T1-T2 loop forms, any genes in that loop region which had been expressing C1/C2 sequences in their 3'UTRs, now cease expressing the C1/C2 sequences. The connectrons formed by these C1/C2 sequences will cease to exist after some time thus opening up the genes inside the respective T1-T2 loops

to expression. The hierarchy of connectron action is alternates between repression and expression. The connectron hierarchies can be of any depth.

5 One-to-Many connectron action – One C1/C2 sequence can form connectrons in many different places on many different chromosomes. The only requirement is that C1=T1 and C2=T2. This makes it possible for one expression event to control the expression of many genes on different chromosomes.

10 Many-to-One connectron action – C1/C2s that come from many different places on many different chromosomes can form a connectron for a specific T1-T2 sequence pair. The only requirement is that C1=T1 and C2=T2. This makes it possible for many different expression events to control the expression of one set of genes on a particular chromosome.

15 Many-to-Many connectron action – The arrangement of C1/C2s and T1-T2s across chromosomes can form a complex web of gene expression control relationships.

20 Percentage of the Genome Regulated by Connectrons – Since the connectrons for a sequenced genome can be calculated, the percentage of the genome that is open to connectron regulation can be known.

25 Emergent Property – The network of connectrons in any genome emerges from a knowledge of the complete DNA sequence of the genome. Because both the C1/C2 sequences and the T1-T2 sequences can be any place in the genome, the whole genomic sequence must be known before all the connectrons can be determined.

30 Paradigm Shift – For the past fifty years since the discovery by Watson and Crick of the double-helical nature of DNA, the reigning paradigm for scientific discovery has been the study of one gene and its effects on the behavior of a cell. The advent of genomic sequencing and this invention of connectrons that emerge from the whole genome will produce a shift in the way scientists view biological systems and the way they formulate and execute experiments. The many-to-many relationships between

the connectrons means that there are many ways in which the expression of a set of genes can be modulated. The multiplicity of control pathways means produces a system stability that makes it possible for biological systems to be stable for long periods of evolutionary time. The thinking that goes into formulating scientific experiments will have to change to accommodate the changes in understanding that will be induced by the application and extension of this patent application.

Hierarchy of DNA Structuring – The DNA of a cell's genome is structured in a hierarchy of six levels. Figures 1, 2 and 3 have been adapted from The Molecular Biology of the Cell by Alberts, Bray, Lewis, Raff, Roberts and Watson [third edition pages 354, 345 and 348]. As shown in figure 1, the double stranded DNA is level 1. The double-stranded DNA is wrapped around histone proteins to form a chromatin particle that is level 2 of the hierarchy. Level 2 is described as "beads-on-a-string" in figure 1. The chromatin particles are packed in a six-fold symmetry as shown in figure 2a and figure 2b. These six-fold assemblies have a diameter of 30 nm. Each 30 nm assembly contains from 18 (i.e. $6 * 3$) to 30 (i.e. $6 * 5$) chromatin particles. The 30 nm assemblies aggregate into large loops which range in length from 5,000 bases to 100,000 bases of DNA. The size of these large loops as shown in figure 1 is approximately 300 nm. These large loops constitute level 4 of the structuring hierarchy. As shown in figure 1, level 5 of the DNA structuring hierarchy many large loops are condensed to form a structure which is approximately 700 nm in diameter. The complete chromosome that constitutes level 6 of the hierarchy is composed of two very long sections of level 5 DNA.

Model of Chromatin Structure – The level 4 structure of DNA as shown in figure 1 ranges in length from 5,000 to 105,000 bases of DNA. Figure 3 shows that proteins are thought to connect portions of the long loops formed by the 30 nm particles to form a chromosome axis. These condensed long loops are described as chromomeres in The Molecular Biology of the Cell.

Prior Art

The chromomere model of DNA structuring was presented by N. A Resnik, et al.[1] and is based on electron microscopic data. There are more recent papers studying a variety of genomes with electron microscopy but no equivalent study of chromomeres has been done on a fully sequenced genome.

A recent News Feature in Nature by T. Gura [2] described the discovery of post-transcriptional gene silencing in which viral RNA interacts with the transcribed RNA of the cell to silence the expression of genes. This article describes experiments in C. elegans and D. megalomaster in which RNA that is complementary to mRNA introduced into a cell. This "antisense" RNA has the effect of turning off the expression of one or more genes. The introduced complementary RNA produces an "RNA interference" called RNAi.

Thomas Werner and his colleagues at Genomatix in Munich, Germany have developed an approach to understanding what they call "Matrix Attachment Region" (MAR). Figure 5 shows their interpretation of the structure of DNA surrounding a gene. The following description of the MAR is copied from the Genomatix web site

"Matrix Attachment Regions (MARs) MARs are sequence regions that are responsible for the attachment of genomic DNA to the nuclear matrix or scaffold. Transcription absolutely requires anchorage of genomic DNA to the nuclear matrix.

Functional features of MARs:

Anchoring of regulatory elements like promoters and enhancers to the nuclear matrix.

Ensuring long term activity of promoters and enhancers in chromatin.

Insulation, rendering a functional domain insensitive to position effects.

Genomatix is conducting a research project to define and detect MARs by computer-analysis."

Brief Description of the Objects of the Invention

An object of the invention is to provide a method of identifying DNA sequences that
5 control the expression of different collections of genes in a genome comprising,
detecting selected DNA sequences adjacent to some genes excluding exons and
introns.

An object of the invention is to provide a method of identifying DNA sequences that
10 control the expression of different collections of genes comprising, detecting, by
computer, one or more pairs of non-adjacent DNA sequences to which are bound to
two RNA sequences.

An object of the invention is to provide a method of identifying DNA sequences that
15 control the expression of different collections of genes in a genome comprising
detecting changes in connectron behavior in the genome.

An object of the invention is to provide a method of modifying the expression of
different gene collections in a genome, comprising detecting changes in connectron
20 behavior as a result of an exogenous stimulus.

An object of the invention is to provide a method of detecting where and when new
genes are being integrated into a host genome comprising detecting the connectrons in
said host genome.

An object of the invention is to provide a method of detecting the expression effect of
different gene collections in a given body comprising detecting the back and forth
flow of connectrons between the chromosomes thereof.

An object of the invention is to provide a method of modifying a given body comprising modifying the connectron organization therein.

An object of the invention is to provide a method of detecting connectron control and
5 target sequences in a given genome comprising:

determining the base composition of said genome,
determining one or more sites of control sequence organization, and/or
determining one or more sites of target application.

10 An object of the invention is to provide a method of determining the response of a cell in any tissue to changes in the cell's environment and/or genetic composition comprising providing a complete genomic DNA sequence for the organism and determining the effect of changes in connectrons due to application of a given
15 exogenous stimulus to the genome.

An object of the invention is to provide a method of determining in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes, the tetradic relationship
20 T1=C1 and T2=C2 where T1 and T2 are DNA sequences 20 or more bases in length, where the C1 sequence is adjacent to the C2 sequence, where the T1 and T2 sequences are on the same chromosome, and where the C1/C2 sequences are on the same chromosome as T1 and T2 or where the C1/C2 sequences are on a chromosome different from T1 and T2, wherein:

25 C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

30 C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

5 T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence; the T1 and T2 sequences must be between about 1kb and 105kb apart, and

10 T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

15 An object of the invention is to provide a method of determining in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes, the connectron relationship that permits many different C1/C2 short loops to control the existence of a T1-T2 long loop and wherein said C1/C2 short loops can be on the same chromosome or on different chromosomes from the T1-T2 long loop, wherein:

20 C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

25 C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

30 C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

5 An object of the invention is to provide a method of determining in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes, the connectron relationship that permits one C1/C2 short loop to control the existence of many T1-T2 long loops, the C1/C2 short loop can be on the same chromosome or on different chromosomes from the T1-T2 long loops, wherein:

10 C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

15 C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

20 C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

25 T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

30 An object of the invention is to provide a method of determining in the connectron relationships between prokaryotes and their plasmids wherein said connectrons implement a control mechanism between the two genomes that makes it possible from

them to form a symbiotic relationship, and in the case of *D. radiodurans* the relationship is not symmetric, and the *D. radiodurans* genome sends C1/C2 short loops to the MP1 plasmid, wherein:

5 C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

10 C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

15 C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

20 T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

25 T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

An object of the invention is to provide a method of determining that connectron relationships that exist in plant and higher animals.

30 An object of the invention is to provide a method of determining in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes, the connectron relationship that permits one C1/C2 short loop to control the existence of one or more T1-T2 long loops without being subject to any expression controls other than those of the gene to which the C1/C2 is 3'UTR, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

5 C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

10 C1/C2 - any positive or negative strand DNA sequence of 540 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart,

15 T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart, and

20 3'UTR - untranslated 3' end of an mRNA is beyond the end of the last exon, a stop codon in the mRNA causes the ribosome to stop the translation of mRNA into protein.

25 An object of the invention is to provide a method of determining in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes, the connectron relationship that permits one C1/C2 short loop to control the existence of one or more T1-T2 long loops such that this C1/C2 short loop is itself subject to expression control by another T1-T2 long loop which surrounds it, wherein:

30 C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

5

C1/C2 - any positive or negative strand DNA sequence of 540 or more bases such that the C1 sequence is adjacent to the C2 sequence,

10

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

15

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

20

An object of the invention is to provide a method of determining in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes, the connectron relationship that permits one C1/C2 short loop to control the existence of the T1-T2 long loop that surrounds it, wherein:

25

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

30

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

5 T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

An object of the invention is to provide a method of determining the connectron
10 relationships that do not have any genes within the T1-T2 long loop, wherein:

T1 sequence is any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, and

15 T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, and the T2 or T1 sequences must be between about 1kb and 105kb apart.

An object of the invention is to provide a method of determining the geneless
20 connectron relationship where one C1/C2 short loop controls the existence of many
 geneless T1-T2 long loops, wherein:

25 C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

30 C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

5

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

Description of the Drawings and Tables

The above and other objects, advantages and features of the invention will become more apparent when considered with the following specification and accompanying drawings and tables wherein:

Figure 1 DNA is structured in six levels of increasing condensation. Double stranded DNA is level 1. Two turns of DNA are wrapped about each chromatin particle at level 2. The chromatin particles which each containing 200 base pairs form into 30 nm particles at level 3. The 30 nm particles form into large loops with an approximate dimension of 300 nm at level 4. Metaphase chromosomes form a condensed structure with an approximate dimension of 700 nm at level 5. An entire metaphase chromosome has a width of approximately 1400 nm at level 6. The large loops at level 4 of the DNA structuring are thought to have between 20,000 (20 kb) and 100,000 (100 kb) base pairs.

The Molecular Biology of the Cell by Alberts, Bray, Lewis, Raff, Roberts and Watson, 3rd. ed. , Garland Publishing, Inc., New York, 1994, p. 354

Figure 2 (a) Chromatin DNA forms into a six-fold symmetry 30nm particles.
(b) The six-fold symmetry 30nm particles form a linear chain with a varying number of repeat units.

The Molecular Biology of the Cell by Alberts, Bray, Lewis, Raff, Roberts and Watson , 3rd. ed. , Garland Publishing, Inc., New York, 1994, p. 345

Figure 3 Long loops of 30nm particles are thought to be closed at the bottom of the loop by proteins.

5 The Molecular Biology of the Cell by Alberts, Bray, Lewis, Raff, Roberts and Watson, 3rd. ed. , Garland Publishing, Inc., New York, 1994, p. 348

Figure 4 (a) Transcription and Editing. (b) Movement of the RNA through the Nucleus. (c) Connectron Formation

10 Figure 5 Overview of schematic organization of a typical transcriptionally active chromosomal loop.

From http://genomatix.gsf.de/func_genomics/functional_genomics.html

15 Table 1 Connectron Properties for Prokaryotic, Archea and Eukaryotic Genomes

Table 2 Yeast Inter-Chromosomal Connectron Distribution

Figure 6 Genome size plotted as a log-log function of the Number of Connectrons

Figure 7 Number of Sequence Instances plotted as a function of the Number of Fragments

5 Figure 8 Level 0 – The overall view of the algorithm

 Figure 9 Level 1 – Process Flow of the Algorithm

 Figure 10 Level 2a – two pages – Process Genome into Blocking Fragment File

 Figure 11 Level 2b – two pages – Compute the Connectrons for a Genome

 Figure 12 Level 2c – two pages – Analyze Possible Connectrons

10 Figure 13 Level 3a – Setup Genome Usage Memory

 Figure 14 Level 3b – Find DBP-Size Blocking File for T1-Window

 Figure 15 Level 1 – Find DBP-Size Blocking File for T2-Window

 Figure 16 Level 2a – two pages – Find C1/C2 Entries

15 Figure 17 Level 2b – two pages – Scan Genome Usage Memory for Potential Connectrons

Description of the Invention

A connectron is a relationship among four DNA sequences. Each sequence must be at least 20 bases long. There is a report by Sharp and Zamore [3] that RNA sequences of "about length 25" are important as sources of RNAi. 27 bases were actually used as the minimum length of each of the sequences. The T1 sequence is on one strand of some chromosome in a genome. The T2 sequence is on the same strand of the same chromosome as the T1 sequence. The T1 and T2 sequences (which are each at least 20 bases in length) must be at least 5,000 bases distant from each other but they can not be more than 105,000 bases distant from each other. The C1 sequence and the C2 sequence (which are each at least 20 bases in length) are adjacent to each other on some strand of some chromosome in the genome. The C1/C2 sequences – called the "short loop" – can be on the same strand as the T1 and T2 sequences or they can be on the opposite strand. The C1/C2 sequences of the short loop can be on the same chromosome as the T1 and T2 sequences but they can also be on a different chromosome in the genome. When a genome has only one chromosome, then the point is moot. Many genomes, of course, have several chromosomes. The C1 sequence is identical to the T1 sequence and the C2 sequence is identical to the T2 sequence.

The C1/C2 sequence must be on the same strand as a gene, either be directly adjacent to the gene (i.e. a gap of 0 bases) for prokaryotic genomes or at this time be within 10,000 bases for eukaryotic genomes. The size of the gap between the end of the gene and the beginning of the C1/C2 sequence is a variable. The C1/C2 short loop is expressed as the 3'UTR (Un-Translated Region) of the gene. In the case of prokaryotic genes that do not normally have introns, the whole mRNA becomes the active species for connectron formation. In the case of eukaryotic genes, the whole transcript is the active species for connectron formation upon editing of the transcript to eliminate the introns. The whole transcript then can move about in the cytoplasm of prokaryotic cells or the nucleus of eukaryotic cells. Since the C1 sequence is equivalent to the T1 sequence and the C2 sequence is equivalent to the T2 sequence,

the C1 RNA can form a Hoogsteen triple-stranded RNA/DNA/DNA helix with the double-stranded T1 sequence. Similarly the C2 RNA can form a Hoogsteen triple-stranded RNA/DNA/DNA helix with the double-stranded T2 sequence. Because the C1 sequence and the C2 sequence are adjacent to each other, the C1/T2 5 RNA/DNA/DNA Hoogsteen triple helix is brought into physical adjacency to the C2/T2 RNA/DNA/DNA Hoogsteen triple helix. RNA/DNA/DNA hybrid helices are the most stable form of triple helix. RNA double helices, DNA double helices, RNA triple helices and DNA triple helices are all significantly less stable than a RNA/double-stranded DNA triple helix. The stable physical adjacency of the two 10 triple-stranded Hoogsteen helices ensures that the long loop of double-stranded DNA between the T1 sequence and the T2 sequence can then be structured into 30 nm chromatin particles as shown in level 4 of figure 1. The genes on either strand of the DNA between the T1 sequence and the T2 sequence when they are structured into the 30 nm chromatin particles are not open to promotion and expression.

15 The tetradic relationship between the T1 and T2 sequences that form the long loop and the C1/C2 sequences that form the short loop are called a connectron. The name "connectron" was suggested by J. David Rawn Ph.D. of Towson University. A connectron is possible if the T1, T2, C1 and C2 sequences exist. A connectron is real 20 if the C1/C2 short loop sequence is adjacent to an expressible gene. If the expression of the adjacent gene is inside one or more T1 – T2 long loops then this connectron is said to be transient. If the adjacent gene is not inside any possible T1-T2 long loop then the connectron is said to be permanent. If a connectron is inside of a T1-T2 long loop that has the same sequences (i.e. T1 is really equal to C1 and T2 is really equal 25 to C2) then the connectron is said to be self-limiting. This is true because once the C1/C2 sequence is expressed it forms the T1-T2 long loop that then shuts off the expression of the gene adjacent to the C1/C2 sequence. Self-limiting connectrons can also be called "spike" connectrons since they generate a short-duration spike of the C1/C2 short loop sequence. If a T1-T2 long loop does not contain any genes but it 30 contains C1/C2 short loop sequences then this type of connectrons is said to be geneless. The C1/C2 short loops within a geneless T1-T2 long loop can, of course, control the expression of genes.

The physical existence and lifetimes of the connectrons must be proved by molecular biological experimentation. This physical experimental process, however, is logically quite separate from the computational experimentation that have been conducted
5 from June of 1999 to May of 2001. The computational search for the existence of connectrons has been extremely positive. These computations have shown that connectrons exist in prokaryotes, in archea, between prokaryotes and their plasmids, in single-celled eukaryotes, in multi-celled eukaryotes, in plants, in higher animals and in humans. All of these features and properties are described in the claims
10 section that follows.

The connectron invention is very powerful. It depends only on sequence equivalency. The minimum length of the four sequences seems to be about 20 bases. In the calculations shown in this patent application, 27 bases have been used as a minimum.
15 The Nature News Feature [1] says that other scientists have found RNA sequences of length about 25 that have interesting gene silencing properties. The Nature article does not give any mechanism. Because of my algorithm and its use on a variety of genomes, this patent application provides the computational proof that a particular mechanism is highly probable. The connectron invention provides an explanation for
20 how communication occurs with a chromosome as well as between chromosomes in genomes that have more than one chromosome. Since each T1-T2 long loop can contain one or more genes, the connectron invention provides a mechanism for turning on and turning off sets of genes simultaneously. In time, the connectron invention will provide an explanation for how differentiation of how one cell's behavior differs from the behavior of another adjacent cell. It is already clear from
25 the computational experiments that have been made on *S. cerevisiae*, *C. elegans* and *D. megalomaster* that the number of geneless connectrons increases dramatically as evolution proceeds from single-celled eukaryotes (i.e. *S. cerevisiae*) to 1,000 cell eukaryotes (i.e. *C. elegans*) to visible creatures (i.e. *D. megalomaster*). The extension
30 of this evolutionary progress to plants (i.e. *A. thaliana*) for which only three chromosomes are sequenced and humans (i.e. *H. sapiens*) for which only one chromosome is completely sequenced. Although the complete human genome was

published in Nature and Science in February of 2001, the NIH-sponsored genomic sequencing results are available for about 1/3 of the bases in the whole genome. The human genomic sequence determined by Celera Genomics, Inc. is available only by subscription. Table 1 shows how the genome size, the number of genes, the number of gene-containing and geneless connectrons and the percentage of genes controlled are related in many different genomes.

The C1/C2 short loops originate on one chromosome. The T1-T2 long loops can be on the same or different chromosomes. Table 2 which is for yeast (*S. cerevisiae*) is a square matrix of how many C1/C2 short loops on a given chromosome are sent to form T1-T2 long loops on other chromosomes. The diagonal of this matrix shows that many chromosomes send connectrons to themselves. The striking feature of this particular table is that chromosome 6 only sends connectrons to chromosome 12 but that it receives connectrons from chromosomes 4,5,7,10,12,13,15 and 16.

Any tetrad of connectron sequences (i.e. the T1, T2, C1 and C2 sequences) as well as the fact of the adjacency of the C1/C2 short loop sequence to the transcribing gene can be patented because the content of matter and the utility can be exactly described. The utility of a connectron is that the T1-T2 long loop shuts off the expression of the genes that lie between the T1 sequence and the T2 sequence. In the case of geneless connectrons, the utility is of a higher level in that the C1/C2 short loops contained in the higher-level geneless T1-T2 long loop, eventually form other lower-level T1-T2 long loops around a set of genes.

The invention of connectrons comes at a particularly important time in biological discovery. The geneless connectrons make a many-to-many hierarchical control mechanism possible. It is already clear from the determination of the connectrons for *C. elegans* and *D. melangaster* that there are as many or more geneless connectrons than there are genes. It has been clear for some time that the number of genes in a genome is not particularly correlated with the size of the genome. Figure 6 shows that the size of a genome is roughly linearly correlated with the number of connectrons.

The connectron invention can be used to generate a model of behavior in any cell. The simulation of connectron behavior in different genomes will be the subject of another patent application.

5

The connectron invention provides for a rational exploitation of the information contained in the raw genomic DNA sequence by forming a hierarchy of relationships between geneless connectrons, transient connectrons, permanent connectrons, self-limiting connectrons and the expression of genes.

10

Detailed Description of the Invention

The algorithm for the determination of connectrons in any genome or any genome fragment is represented in the following flow diagrams. The Level 0 diagram in figure 8 shows the general relationships in a digital computer. The central processor of the digital computer uses the computer program to take genome descriptors, the genomic DNA sequences and the tables of gene features to produce a file of blocking fragments and a file of the optimal connectrons for the genome. The printer serves to make hard copies of the files and this patent application. The level 1 diagram in figure 9 shows the three essential steps in the determination of connectrons. The genome is first processed into a blocking fragment file. Then the blocking fragments are used to compute the connectrons for the genome. Finally the potential connectrons are analyzed to determine if the C1/C2 sequences are in the 3'UTR of a gene. The level 2a diagram in figure 10 shows the steps required for the processing of the genome into a file of blocking fragments. The genomic DNA sequence is decomposed into 27-base frames for both the positive and negative strands. These fragments are written to the unsorted fragment file. The fragment file is then sorted is then read and formed into groups of equivalent sequences. The (.blk) file contains the sequence and a pointer to the (.gptr) file which contains the pointers to the position of the fragments in the genomes. The position in the genome includes the chromosome number, the position in the chromosome and the strand (i.e. positive and negative). A sample of these files follows

25 Sample of the (.blk) file for *S. cerevisiae*

27-base fragment	Number of instances	Pointer to (.gptr) file
------------------	------------------------	----------------------------

11111111111111111111111111	0	1
111111123244233313332443414	1	2
111111141113443133314333341	2	4
111111232442333133324434141	1	5
111111323311133323144423444	2	7
11111132213331341414443413	2	9
111111333444112343412323243	1	10

	111111333444113343412323243	9	19
	111111411134431333143333414	2	21
5	111111443223134142124434124	2	23
	11111222323434444443144442	2	25
	111112244123441122214421213	8	33
	111112311241114344334134431	2	35
	111112324423331333244341414	1	36
10	111112344232231344242234342	1	37
	111112433444244421144134211	1	38
	111112444311313442332142224	1	39
	111113131241131114424413231	1	40
	111113143332344311113133411	1	41
	111113233111333231444234441	2	43

15 In fragments above 1=G, 2=C, 3=A, 4=T

Sample of the (.gptr) file for *S. cerevisiae*

20 There are 16 chromosomes in *S. cerevisiae*

	Item	Chromosome	Position	Direction
			in Chromosome	
25	1	0	0	
	2	4	11137	1
	3	12	467619	1
	4	12	458482	1
	5	4	11138	1
	6	12	465759	2
30	7	12	456622	1
	8	1	219366	1
	9	8	539978	1
	10	14	522451	1
	11	4	1099073	1
35	12	4	1210003	1
	13	7	539068	1
	14	12	654136	1
	15	12	596455	1
	16	15	121016	1
40	17	15	598127	2
	18	16	847724	1
	19	16	59765	1
	20	12	467620	1
	21	12	458483	1
45	22	12	461657	1
	23	12	452520	1
	24	13	838006	1

	25	15	288270	1
	26	4	83593	1
	27	4	992867	1
	28	6	162265	1
5	29	7	845687	1
	30	10	531560	2
	31	15	282208	1
	32	16	860418	1
	33	16	572308	1
10	34	12	465992	1
	35	12	456855	1
	36	4	11139	1
	37	8	89343	1
	38	4	10302	1
15	39	1	19894	2
	40	16	9311	1
	41	10	735203	1
	42	12	465760	1
	43	12	456623	1

20

In direction column above 1=positive strand, 2=negative strand

The level 2b diagram in figure 11 shows the computation of the connectrons. The genome descriptors consist of the number and length of the chromosomes. The algorithm uses an array that represents several facts about each base position in the genome. The level 3a diagram in figure 13 shows the setup of the Genome-Usage memory. The gene features are used to prevent the region of the genome that codes for proteins from being used for the connectron sequences (i.e. the T1s, the T2s, the C1s and the C2s). In the level 2a diagram of figure 10, the algorithm steps through each chromosome and within each chromosome through each base position looking for acceptable T1-windows of 27 bases. A T1-window can be used to form a connectron relationship if there are two or more instances of this fragment in the blocking fragment file. The computation in the level 3b diagram of figure 14 determines if the T1-window is acceptable or not. Once an acceptable T1-window is found, the algorithm (in the level 2a diagram of figure 10) looks for acceptable T2-windows that lie between 5,000 and 105,000 bases from the T1-window. The computation for determining acceptable T2-window positions is done in the level 3c diagram of figure 15. Once a pair of T1 and T2 window positions are found, the

algorithm looks among the instances of these T1 and T2 sequences for a pair of sequences C1 and C2 that lie within 200 bases of each other on the same chromosome. The computation for determining acceptable C1/C2 windows is shown in the level 3d diagram in figure 16. In the level 3e diagram of figure 17 the Genome-Usage memory is scanned for the Possible-Connectrons. In the level 2c diagram of figure 12 the Possible-Connectrons are scanned to determine if the C1/C2 sequences are within the Gap-Distance of a gene on either the positive or the negative strands. The Real-Connectrons are then written out in several different files including the descriptions in the claims section.

10

Examples

The algorithm for the determination of optimal connectrons has been applied to a number of different publicly available genomes. The connectron is a tetradic relationship between four sequence elements - T1, T2, C1 and C2. The claims presented in this section are written by the program NearGene that implements the flow diagram Level 2c of figure 12. The examples are written a uniform type of English. Each example contains some or all of the following elements

10 Name of genome
 Description of T1
 Length of T1-T2 loop
 The chromosome on which the T1-T2 loop exists
 The identifier number within the genome of the T1 sequence

15 The T1 sequence
 Description of T2
 The identifier number within the genome of the T2 sequence
 The T2 sequence
 A list of genes whose expression is controlled by the T1-T2 loop

20 The common names of the genes as obtained from the NCBI gene feature file (.ptt)
 A list of C1/C2 short loops whose expression is controlled by the T1-T2 loop
 The chromosome on which the C1/C2 short loop exists
 The common name of the gene which expresses the C1/C2 short loop as an RNA

25 The sequence of the C1/C2 short loop
 A list of C1/C2 short loops that control the formation of the T1-T2 loop
 The chromosome on which the C1/C2 short loop exists
 The common name of the gene which expresses the C1/C2 short loop as an RNA

30 The sequence of the C1/C2 short loop

The match between the C1/C2 sequence and the T1 sequence
The match between the C1/C2 sequence and the T2 sequence

5

The uniform descriptions make it possible to rapidly comprehend the specifics in each example.

When a sequence element is very long a series of four dots has been inserted between the beginning and ending sequence groups. A variable number of bases have been deleted.

10

Index of Pages for Connectron Samples**Page 39**

1. Connectrons occur in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes.

5

Page 57

2. Many Connectrons control the expression of one set of genes in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes.

10

Page 83

3. One connectron controls the expression of many sets of genes in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes.

15

Page 107

4. Connectrons occur between prokaryotes and their plasmids.

20

Page 117

5. Connectrons occur in plants and higher animals

25

Page 126

6. Permanent connectrons exist in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes.

30

Page 135

7. Transient connectrons exist in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes.

Page 152

8. Self-limiting connectrons occur in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes

Page 164

9. Geneless connectrons exist in single-celled and multi-celled eukaryotes

5

Page 174

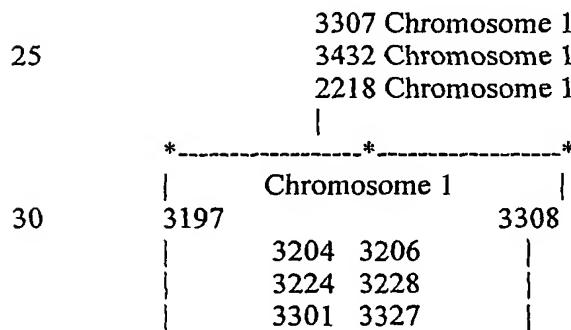
10. One connectron controls many geneless connectrons in single-celled and multi-celled eukaryotes

1. Connectrons occur in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes.

5 Connectrons exist as tetradic relationships where the sequence T1 is equivalent to the sequence C1 (written T1=C1) and where the sequence T2 equals the sequence C2 (written T2=C2) where T1 and T2 are DNA sequences 20 or more bases in length, where the C1 sequence is adjacent to the C2 sequence, where the T1 and T2 sequences are on the same chromosome, and where the C1/C2 sequences are on the same chromosome as T1 and T2 or where the C1/C2 sequences are on a chromosome
10 different from T1 and T2. The connectron relationship has been found to exist in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes.

Example of a prokaryote connectron – E. coli

15 In this example the existence of the T1-T2 (3197-3308) long loop is controlled by three C1/C2 short loops (3307, 3432 and 2218). The T1-T2 long loop controls the expression of 64 genes on chromosome 1 in addition to six C1/C2 (3204, 3206, 3223, 3228, 3301 and 3327) short loops. The C1/C2 short loop 3327 lies outside the range
20 of the T1-T2 long loop (3197-3308) but this C1/C2 is expressed as a 3'UTR to the gene hemG that is within the range of the T1-T2 long loop.



35 -----

Connectron control elements for chromosome 1 of the E. coli genome

5 A double stranded DNA loop of length 93.542 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 3197. This T1 control element has the DNA sequence

AAAAAAATGCGCGGTAGAAAATTATTTAAATTTCCTCTGTCAGGCCGG
 AATAACTCCCTATAATGCGCCACCACTGACACGGAACAACGGCAAACACG
 10 CCGCCGGGTCAAGCAGGGTTCTCCTGAGAACTCCGGCAGAGAAAGCAAAA
 ATAAATGCTTAGCTGTAGCGGGAA

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 3308. This T2 control element has the DNA sequence

15 TAAATTCCTCTGTCAGGCCGGAATAACTCCCTATAATGCGCCACCACTG
 ACACGGAACAACGGCAAACACGCCGCCGGTCAGCGGGGTTCTCCTGAG
 AACTCCGGCAGAGAAAGCAAAAATAATGCTTAGCTGTAGCGGGAAAG
 GCGTATTATGCACACCCCGCGCCGCT

20 This long T1/T2 double stranded DNA loop modulates the expression of the following genes

	rrsC	gltU	rrlC	rffC	aspT	trpT	yifA	yifE	yifB
25	ilvL	ilvG_1	ilvM	ilvE	ilvD	ilvA	ilvY	ilvC	ppiC
	b3776	rep	gppA	rhlB	trxA	rhoL	rho	rfe	wzzE
	wecB	rffH	wecD	wecE	wzxE	yifM_2	wecG	yifK	
	argX	hisR	leuT	proM	aslB	aslA	hemY	hemX	
	hemD	cyaA	cyaY	b3808	dapF	uvrD	b3814	corA	
30	yigF	yigG	rarD	yigI	pldA	recQ	yigJ	yigK	pldB
	yigL	yigM	metR	metE	ysgA	udp	yigN	ubiE	yigP

b3836 yigU yigW_1 rfaH yigC ubiB fadA fadB
pepQ trkH hemG

5 This long T1/T2 double stranded DNA loop modulates the expression of the
following C1/C2 short loops

10 A C1/C2 short loop on chromosome 1 whose identifier is 3204 controls the
expression of the genes of one or more other T1/T2 long loops. This C1/C2 short
loop is expressed as a RNA single strand that is 3'UTR to the gene rrsC and has the
DNA sequence

15 GATGTGCCAGATGGGATTAGCTAGTAGGTGGGTAACGGCTCACCTAGG
CGACGATCCCTAGCTGGTCTGAGAGGATGACCAGCCACACTGGAAGTGAG
ACACGGTCCAGACTCCTACGGGAGGCAGCAGTGGGAATATTGCACAATG
GGCGCAAGCCTGATGCAGCCATGCCGCGTGTATGAA

20 A C1/C2 short loop on chromosome 1 whose identifier is 3206 controls the
expression of the genes of one or more other T1/T2 long loops. This C1/C2 short
loop is expressed as a RNA single strand that is 3'UTR to the gene rrsC and has the
DNA sequence

25 GTCCCCTCGTCTAGAGGCCAGGACACCGCCTTACGGCGGTAAACAG
GGGTTCGAATCCCTAGGGGACGCCACTGCTGGTTGTGAGTCAAAGTC
ACCTGCCTTAATATCTCAAAACTCATCTCGGGTATGTTGAGATATTG
CTCTTTAAAAATCTGGATCAAGCTGAAAATTGAAA

30 A C1/C2 short loop on chromosome 1 whose identifier is 3223 controls the
expression of the genes of one or more other T1/T2 long loops. This C1/C2 short
loop is expressed as a RNA single strand that is 3'UTR to the gene rrlC and has the
DNA sequence

GCTGAAGTAGGTCCCAAGGGTATGGCTGTCGCCATTAAAGTGGTACGC
GAGCTGGTTAGAACGTCGTGAGACAGTCGGTCCCTATCTGCCGTGGG
CGCTGGAGAACTGAGGGGGCTGCTCCTAGTACGAGAGGACCGGAGTGG
ACGCATCACTGGTGGTTCGGGTTGTCATGCCAATGGCA

5

A C1/C2 short loop on chromosome 1 whose identifier is 3225 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene rrlC and has the DNA sequence

10

AAACAGAATTGCTGGCGGCCGTAGCGCGGTGGTCCCACCTGACCCCAT
GCCGAACTCAGAAGTGAAACGCCGTAGCGCCGATGGTAGTGTGGGTCTC
CCCATGCGAGAGTAGGAACTGCCAGGCATCAAATTAAAGCAGTA

15

A C1/C2 short loop on chromosome 1 whose identifier is 3228 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene rrfC and has the DNA sequence

20

GGTCATAAAACCGGTGGTTGTAAAAGAATTGGAGCGGTAGTCAGT
CGGTTAGAATACCTGCCTGTCACGCAGGGGGTCGCGGGTCGAGTCCCGT
CCGTTCCGCCAC

25

A C1/C2 short loop on chromosome 1 whose identifier is 3301 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene ubiB and has the DNA sequence

30

TTATCGTGCCTACAAATAGTCCGAACCGTAGGCCGGATAAGGCAGTTACG
CCGCATC

A C1/C2 short loop on chromosome 1 whose identifier is 3307 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene fadA and has the DNA sequence

5

TGCCGGATGCGCGTAAACGCCTATCCGGCCTACGGTCGGACTATTGT
AGGCA

A C1/C2 short loop on chromosome 1 whose identifier is 3327 controls the
10 expression of the genes of one or more other T1/T2 long loops. This C1/C2 short
loop is expressed as a RNA single strand that is 3'UTR to the gene hemG and has the
DNA sequence

15 AAAAAATGCGCGGTCAAGAAAATTATTTAAATTTCCTCTTGTCAAGGCCGG
AATAACTCCCTATAATGCGCCACCACTGACACGGAACAAACGGCAAACACG
CCGCCGGGTCAAGCGGGTTCTCCTGAGAACTCCGGCAGAGAAAGCAAAA
ATAAAATGCTTGACTCTGTAGCGGGAAGGCGTATTATG...CCCGTCACACCA
TGGGAGTGGGTTGCAAAAGAAGTAGGTAGCTAACCTTCGGGAGGGCGCT
TACCACTTGTGATTCATGACTGGGTGAAGTCGTAACAAGGTAACCGTA
20 GGGGAAACCTGCGGTTGGATCACCTCCTAACCTAAAGAAGCGTTCTTG

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

25 A C1/C2 short loop on chromosome 1 whose identifier is 3307 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene hemG and has the DNA sequence

30 AAAAAATGCGCGGTCAAGAAAATTATTTAAATTTCCTCTTGTCAAGGCCGG
AATAACTCCCTATAATGCGCCACCACTGACACGGAACAAACGGCAAACACG
CCGCCGGGTCAAGCGGGTTCTCCTGAGAACTCCGGCAGAGAAAGCAAAA
ATAAAATGCTTGACTCTGTAGCGGGAAGGCGTATTATG...CCCGTCACACCA

TGGGAGTGGGTTGCAAAAGAAGTAGGTAGCTAACCTTCGGGAGGGCGCT
TACCACTTGATTCATGACTGGGTGAAGTCGTAACAAGGTAACCGTA
GGGGAACCTGCAGGTTGGATCACCTCCTAACCTAAAGAACGCGTTCTTG

5 The match between the T1 sequence and the C1/C2 sequence is

AAAAAAATGCGCGGTCAAGAAAATTATTTAAATTTCCTCTGTCAGGCCGG
AATAACTCCCTATAATGCGCCACCACTGACACGGAACACGGCAAACACG
CCGCCGGGTCAAGCGGGTTCTCCTGAGAACTCCGGCAGAGAAAGCAAAA
10 ATAAATGCTTGACTCTGTAGCGGGAA

The match between the T2 sequence and the C1/C2 sequence is

TAAATTTCCTCTGTCAGGCCGGAAATAACTCCCTATAATGCGCCACCACTG
15 ACACGGAACAAACGGCAAACACGCCGCCGGTCAGCGGGTTCTCCTGAG
AACTCCGGCAGAGAAAGCAAAAATAATGCTTGACTCTGTAGCGGGAAAG
GCGTATTATGCACACCCCGCGCCGCT

A C1/C2 short loop on chromosome 1 whose identifier is 3432 controls the
20 expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed
as a RNA single strand that is 3'UTR to the gene *btuB* and has the DNA sequence

TGCGCGGTCAAGAAAATTATTTAAATTTCCTCTGTCAGGCCGGAAATAACT
CCCTATAATGCGCCACCACTGACACGGAACACGGCAAACACGCCGCCGG
25 GTCAGCGGGTTCTCCTGAGAACTCCGGCAGAGAAAGCAAAAATAATG
CTTGACTCTGTAGCGGGAAAGCGTATTATGCACACC...ACACCATGGGAGT
GGGTTGCAAAAGAAGTAGGTAGCTAACCTTCGGGAGGGCGCTTACCACT
TTGTGATTGATGACTGGGTGAAGTCGTAACAAGGTAACCGTAGGGGAAC
30 CTGCGGTTGGATCACCTCCTAACCTAAAGAACGCGT

The match between the T1 sequence and the C1/C2 sequence is

TGCGCGGTAGAAAATTATTTAAATTCCCTTCAGGCCGGATAACT
CCCTATAATGCGCCACCACTGACACGGAACAACGGCAAACACGCCGCCGG
GTCAGCGGGGTTCTCCTGAGAACTCCGGCAGAGAAAGCAAAAATAATG
CTTGAECTCTGTAGCGGGAA

5

The match between the T2 sequence and the C1/C2 sequence is

TAAATTCCCTTCAGGCCGGATAACTCCCTATAATGCGCCACCACTG
ACACGGAACAACGGCAAACACGCCGCCGGTCAGCGGGGTTCTCCTGAG
10 AACTCCGGCAGAGAAAGCAAAAATAATGCTTAGCTCTGTAGCGGGAAAG
GCGTATTATGCACACCCCGCGCCGCT

A C1/C2 short loop on chromosome 1 whose identifier is 2218 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed
15 as a RNA single strand that is 3'UTR to the gene clpB and has the DNA sequence

CTTGTCAAGGCCGGATAACTCCCTATAATGCGCCACCACTGACACGGAAC
AACGGCAAACACGCCGCCGGC

20 The match between the T1 sequence and the C1/C2 sequence is

CTTGTCAAGGCCGGATAACTCCCTATAATGCGCCACCACTGACACGGAAC
AACGGCAAACACGCCGCCGGC

25 The match between the T2 sequence and the C1/C2 sequence is

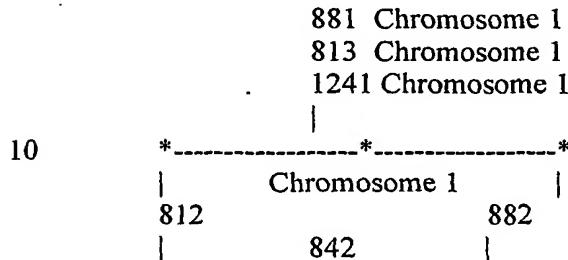
CTTGTCAAGGCCGGATAACTCCCTATAATGCGCCACCACTGACACGGAAC
AACGGCAAACACGCCGCCGGTC

30 -----

Example of an archaea connectron – H. pylori

In this example the existence of the T1-T2 (812-882) long loop is controlled by three C1/C2 short loops (881, 813 and 1214). The T1-T2 long loop controls the expression of 54 genes on chromosome 1 in addition to one C1/C2 (843) short loop.

5



10

Connectron control elements for chromosome 1 of *H. pylori* genome

A double stranded DNA loop of length 96.385 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 812. This T1 control element has the DNA sequence

TTTACTCATAGGGTTTTATAGTCCTAGCGGAACCAAAGCA

25

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 882. This T2 control element has the DNA sequence

TAGCGGAACCAAAGCATTCACTCCAAACACTAAAGATATTG

30

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

HP0999	HP1000	HP1001	HP1002	HP1003	HP1005	HP1006	
HP1008	HP1009	HPtRNA-Pro	HP1010	HP1011	HP1013	HP1015	
35	HP1017	HP1018	HP1020	HP1021	HP1022	HP1023	HP1024

	HP1025	HP1027	HP1028	HP1030	HP1031	HP1033	HP1034
	HP1038	HP1039	HP1040	HP1041	HP1042	HP1043	HP1044
	HP1045	HP1046	HP1051	HP1052	HP1055	HP1056	HP1058
	HP1060	HP1065	HPtRNA-Ser	HP1066	HP1067	HP1069	HP1070
5	HP1074	HP1075	HP1076	HP1077	HP1078	HP1079	HP1080
	HP1081	HP1083	HP1084	HP1085	HP1088	HP1091	HP1092
	HP1093	HP1094	HP1095	HP1096			

10 This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

15 A C1/C2 short loop on chromosome 1 whose identifier is 813 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene HP0998 and has the DNA sequence

TTTACTCATAGGGTTTTATAGTTCTAGCGGAACCTAAAGCATTGATCCC
AAACACTAAAGATATTG

20 The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

25 A C1/C2 short loop on chromosome 1 whose identifier is 881 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene HP1096 and has the DNA sequence

TTTACTCATAGGGTTTTATAGTTCTAGCGGAACCTAAAGCATTGATCCC
AAACACTAAAGATATTG

30 The match between the T1 sequence and the C1/C2 sequence is

TTTACTCATAGGGTTTATAGTCCTAGCGGAACAAAGCA

The match between the T2 sequence and the C1/C2 sequence is

5 TAGCGGAACAAAGCATTCACTCCAAACACTAAAGATATTGG

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

10 A C1/C2 short loop on chromosome 1 whose identifier is 813 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene HP0998 and has the DNA sequence

15 TTTACTCATAGGGTTTATAGTCCTAGCGGAACAAAGCATTCACTCCC
AAACACTAAAGATATTGG

A C1/C2 short loop on chromosome 1 whose identifier is 881 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene HP1096 and has the DNA sequence

20 TTTACTCATAGGGTTTATAGTCCTAGCGGAACAAAGCATTCACTCCC
AAACACTAAAGATATTGG

The match between the T1 sequence and the C1/C2 sequence is

25 TTTACTCATAGGGTTTATAGTCCTAGCGGAACAAAGCA

The match between the T2 sequence and the C1/C2 sequence is

30 TAGCGGAACAAAGCATTCACTCCAAACACTAAAGATATTGG

A C1/C2 short loop on chromosome 1 whose identifier is 1241 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene HP1535 and has the DNA sequence

5 TTTACTCATAGGGTTTTATAGTCCTAGCGGAACAAAGCATTCA
 AACAA

The match between the T1 sequence and the C1/C2 sequence is

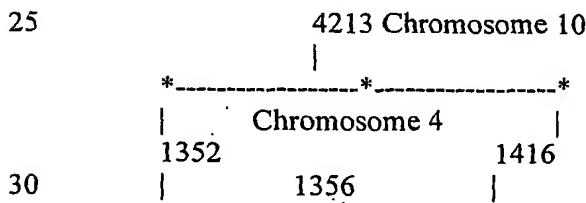
10 TTTACTCATAGGGTTTTATAGTCCTAGCGGAACAAAGCA

The match between the T2 sequence and the C1/C2 sequence is

TAGCGGAACAAAGCATTCA
15 CCCAAACA

Example of single-celled connectron – *S. cerevisiae*

20 In this example the existence of the T1-T2 (1352-1416) long loop on chromosome 4 is controlled by one C1/C2 short loop (4213) on chromosome 10. The T1-T2 long loop controls the expression of 34 genes on chromosome 4 in addition to one C1/C2 (1356) short loop.



Connectron control elements for chromosome 1 of *S. cerevisiae* genome

A double stranded DNA loop of length 68.908 kilo-bases on chromosome 4 is bounded on the left by a T1 sequence whose identifier is 1352. This T1 control element has the DNA sequence

5

TTATGAGAAGCTGTCATCGAAGTTAGAGGAAGCTGAA

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 1416. This T2 control element has the DNA sequence

10

ATTAGATCTATTACATTATGGGTGGTATGTTGGAATAAAATCAACTATCA
TCTACTAACTAGTATTCACGTTACTAGTATATTATCATATACGGTGTAGA
AGATGACGCAAATGATGAGAAATAGTCATCTAAATTAGTGGAAAGCTGAA
ACGCAAGGATTGATAATGTAATAGGATCAATGAATATTAACATATAAAC
15 GATGATAATAATATTATAGAATTGTGTAGAATTGCAGATTCCCTTTATG
GATTCCCTAAATCCTTGAGGAGAACTTCTAGTATATCTACATACCTAATATT
ATAGCCTTAATCACAAATGGAATCCCAACAATTACATCAAAATCCACATTC
TCTACAGTA

20

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

YDR170W-A YDR171W YDR172W YDR173C YDR174W YDR175C
YDR176W YDR177W YDR178W YDR179C YDR179W-A YDR180W
25 YDR181C YDR182W YDR183W YDR184C YDR185C YDR186C
YDR187C YDR188W YDR189W YDR190C YDR191W YDR192C
YDR193W YDR194C YDR195W YDR196C YDR197W YDR198C
YDR199W YDR200C YDR201W YDR202C YDR203W YDR204W
YDR205W YDR206W YDR207C YDR208W YDR209C YDR210W

30

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

A C1/C2 short loop on chromosome 4 whose identifier is 1356 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YDR170W-A and has the DNA sequence

5
AATCACACTAACATTCTGATGATGAACTCCCTGGACACCTCCTCTCGAT
TCAGGAGCATCACGAACCTTATAAGATCTGCTCATCACATACACTCAGC
ATCATCTAACCTGACATAAACGTAGTTGATGCTAAAAAGAAATATAC
10
CAATTAACGCTATTGGTGACCTACAATTCACTTCCAGGACAACACCAA
ACATCAATAAAGGTATTGCACACTCCTAACATAGCCTATGACTTACTCAGT
TTGAATGAATTGGCTGCAGTAGATATCACAGCATGCTTACCAAAAACGT
CTTAGAACG

15
The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

A C1/C2 short loop on chromosome 10 whose identifier is 4213 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YJR029W and has the DNA sequence

20
ATCTATTACATTATGGGTGGTATGTTGGAATAAAAATCCACTATCGTCTAT
CAACTAATAGTTATATTCAATATATTATCATATACGGTGTAAAGATGAT
25
GACATAAGTTATGAGAAGCTGTATCGAAGTTAGAGGAAGCTGAAACGC
AAGGATTGATAATGTAATAGGATCAATGAATATAAACATATAAAACGGA
ATGAGGAATAATCGTAATATTAGTATGTAGAAATATAGATTCCATTTGA
GGATTCCATATCCTCGAGGAGAACTTCTAGTATATTCTGTATACCTAATA
TTATAGCCTTATCAACAAATGGAATCCAAACAATTATCTCAACAT

30
The match between the T1 sequence and the C1/C2 sequence is

TTATGAGAAGCTGTCATCGAAGTTAGAGGAAGCTGAA

The match between the T2 sequence and the C1/C2 sequence is

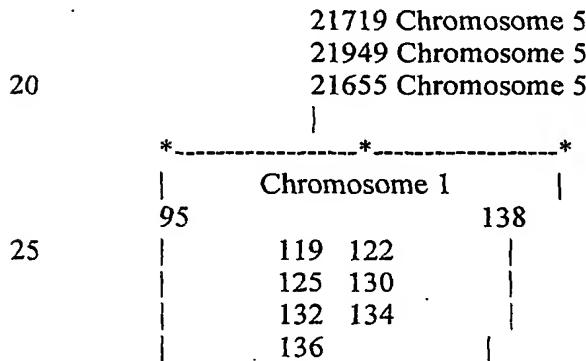
5 ATCTATTACATTATGGGTGGTATGTTGGAATAAAAATC

10

Example of a multi-celled connectron – *C. elegans*

In this example the existence of the T1-T2 (9-138) long loop on chromosome 1 is controlled by three C1/C2 short loops on chromosome 5 (21719, 21949 and 21655).

15 The T1-T2 long loop controls the expression of four genes on chromosome 1 in addition to seven C1/C2 (119, 122, 125, 130, 132, 134 and 136) short loops.



A double stranded DNA loop of length 41.978 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 95. This T1 control element has the DNA sequence

35

CAGCACGTTCTAACCATGCAAAATCAGTTGAGAACTCTGCGTCTCTCTC
CCGC

5 This double stranded DNA loop is bounded on the right by a T2 control element
whose identifier is 138. This T2 control element has the DNA sequence

ACTCTGCGTCTCTCTCCGCATTTTGATAGATCA

10 This long T1/T2 double stranded DNA loop modulates the expression of the
following genes

Y73A3A.1 Y73A3A.1 ZC123.3 ZC123.2

15 This long T1/T2 double stranded DNA loop modulates the expression of the
following C1/C2 short loops

20 A C1/C2 short loop on chromosome 1 whose identifier is 119 controls the expression
of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is
expressed as a RNA single strand that is 3'UTR to the gene ZC123.3 and has the
DNA sequence

TTGAGAACTCTGCGTCTCAACTCCGCATTTTGATCTACGTAGATC
AAACCGAAATGGGACACT

25 A C1/C2 short loop on chromosome 1 whose identifier is 122 controls the expression
of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is
expressed as a RNA single strand that is 3'UTR to the gene ZC123.3 and has the
DNA sequence

30 GCACGGGGTTCTGGCCTTCCTCATTGAATTTCGCGCTCCATTGACAATC
GCCTGCCGGACAACGCGTGGAAAGTCGTACTCCAC

A C1/C2 short loop on chromosome 1 whose identifier is 125 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene ZC123.3 and has the DNA sequence

5

ACGCGCCGTAAATCTACCCCAGATATGGCCGAGCCAAAATGGCCTAGTTC
GGCAAACCTTTCAATTATGAGGGAAGCCAGAA

A C1/C2 short loop on chromosome 1 whose identifier is 130 controls the expression
10 of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is
expressed as a RNA single strand that is 3'UTR to the gene ZC123.2 and has the
DNA sequence

15 CTCCCGCATTTTTGTAGATCTACGTAGATCAAACCGAAATGAGGCACTT
CTGAATCCACGAGCTAGGCTTAAGCTTAGGCTTAAGCTTAGGCCTTTCTC
AGGCTTAGGCTTAGGCTTA

A C1/C2 short loop on chromosome 1 whose identifier is 132 controls the expression
of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is
20 expressed as a RNA single strand that is 3'UTR to the gene ZC123.2 and has the
DNA sequence

25 GCTTATGCTTGGGCTTAGGCTTAGGCGTAGGCTTAGGCTTAGGCTTAGGCT
TATGCTTAGACTTAGTCTCACTATCAGTCTTAGGCTTAGGCTTAGACTTAG
GCTTAAGCTTAGGCTTAAGCTTAGACTTAGGCTTAGGCTTAGGCTTAGGCT
TAGGCTTAGGTTGGGCTTAGGCTTAGGCTTAACCTC

30 A C1/C2 short loop on chromosome 1 whose identifier is 134 controls the expression
of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is
expressed as a RNA single strand that is 3'UTR to the gene ZC123.2 and has the
DNA sequence

TCTGCGTCTTTCTCCGCATTTTGATCTACGTAGATCAAACCGAA
ATGAGGCACCTTCTGAATCCACGAGCTAGGCTTAAGCTTAGGCTTAAGCTT
AGGCCTTTCTCAGGCTTAGGCTTAGGCTTA

5 A C1/C2 short loop on chromosome 1 whose identifier is 136 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene ZC123.2 and has the DNA sequence

10 GCTTATGCTGGGCTTAGGCTTAGGCGTAGGCTTAGGCTTAGGCTTAGGCT
TATGCTTAGACTTAGTCTCACTATCAGTCTTAGGCTTAGGCTAGACTTAG
GCTTAAGCTTAGGCTTAAGCTTAGACTTAGGCTTAGGCTTAGGCTTAGGCT
TAGGCTTAGGTTGGGCTTAGGCTTAGGCTAACCTC

15 The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

A C1/C2 short loop on chromosome 5 whose identifier is 21719 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed
20 as a RNA single strand that is 3'UTR to the gene C39F7.5 and has the DNA sequence

ACGTTCTAACCATGCAAAATCAGTTGAGAACTCTGCGTCTCTCTCCGC
ATTTTTGTAGATC

25 The match between the T1 sequence and the C1/C2 sequence is

ACGTTCTAACCATGCAAAATCAGTTGAGAACTCTGCGTCTCTCTCCGC

The match between the T2 sequence and the C1/C2 sequence is

30 ACTCTGCGTCTCTCTCCGCATTTTGATCTACGTAGATCAAACCGAA

A C1/C2 short loop on chromosome 5 whose identifier is 21949 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene F16B4.4 and has the DNA sequence

5 ACCATGCAAAATCAGTTGAGAACTCTGCGTCTCTCTCCGCATTGGTAG
AGATCTACGTAGATCAAGCCGAAATGAGACACTCTGACACCACG

The match between the T1 sequence and the C1/C2 sequence is

10 ACCATGCAAAATCAGTTGAGAACTCTGCGTCTCTCTCCGC

The match between the T2 sequence and the C1/C2 sequence is

ACTCTGCGTCTCTCTCCGCATTGGTAGATC

15 A C1/C2 short loop on chromosome 5 whose identifier is 21655 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene C39F7.3 and has the DNA sequence

20 AACCATGCAAAATCAGTTGAGAACTCTGCGTCTCTCTCCGCATTGGTAG
ATCTACG

The match between the T1 sequence and the C1/C2 sequence is

25 AACCATGCAAAATCAGTTGAGAACTCTGCGTCTCTCTCCGC

The match between the T2 sequence and the C1/C2 sequence is

ACTCTGCGTCTCTCTCCGCATTGGTAGATC

30

2. Many Connectrons control the expression of one set of genes in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes.

Many different C1/C2 short loops can control the existence of one T1-T2 long loop.

5 The C1/C2 short loops can be on the same chromosome or on different chromosomes from the T1-T2 long loop. This relationship is described as "many-to-one". This relationship exists in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes

10 Example of a many-to-one connectron in prokaryotes – E. coli

In this example the existence of the T1-T2 (3197-3308) long loop is controlled by three C1/C2 short loops (3307, 3432 and 2218).

15 3307 Chromosome 1
 3432 Chromosome 1
 2218 Chromosome 1
 |
 ----------*
 20 | Chromosome 1 |
 3197 3308

25 A double stranded DNA loop of length 93.542 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 3197. This T1 control element has the DNA sequence

30 AAAAAAATGCGCGGTCAAGAAAATTATTTAAATTCCTCTTGTCAAGGCCGG
 AATAACTCCCTATAATGCGCCACCACTGACACGGAACAAACGGCAAACACG
 CCGCCGGGTCAAGGGGTTCTCCTGAGAACTCCGGCAGAGAAAGCAAAA
 ATAAATGCTTGACTCTGTAGCGGGAA

35 This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 3308. This T2 control element has the DNA sequence

TAAATTCCTCTTGTCAAGGCCGGAATAACTCCCTATAATGCGCCACCACTG
 ACACGGAACAAACGGCAAACACGCCGCCGGTCAGCGGGTTCTCCTGAG
 AACTCCGGCAGAGAAAGCAAAAATAATGCTTAGCTCTGTAGCGGAAAG
 5 GCGTATTATGCACACCCCGCGCCGCT

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

10	rrsC	gltU	rrlC	rrfC	aspT	trpT	yifA	yifE	yifB
	ilvL	ilvG_1	ilvM	ilvE	ilvD	ilvA	ilvY	ilvC	ppiC
	b3776	rep	gppA	rhlB	trxA	rhoL	rho	rfe	wzzE
	wecB	rffH	wecD	wecE	wzxE	yifM_2	wecG	yifK	
	argX	hisR	leuT	proM	aslB	aslA	hemY	hemX	
15	hemD	cyaA	cyaY	b3808	dapF	uvrD	b3814	corA	
	yigF	yigG	rarD	yigI	pldA	recQ	yigJ	yigK	pldB
	yigL	yigM	metR	metE	ysgA	udp	yigN	ubiE	yigP
	b3836	yigU	yigW_1	rfaH	yigC	ubiB	fadA	fadB	
	pepQ	trkH	hemG						

20

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

25

A C1/C2 short loop on chromosome 1 whose identifier is 3307 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene hemG and has the DNA sequence

AAAAAAATGCGCGGTCAAGAAAATTATTTAAATTCCTCTTGTCAAGGCCGG
 AATAACTCCCTATAATGCGCCACCACTGACACGGAACAAACGGCAAACACG
 30 CCGCCGGGTCAAGCGGGTTCTCCTGAGAACTCCGGCAGAGAAAGCAAAA
 ATAAATGCTTAGCTCTGTAGCGGGAAAGGCGTATTATG...GGAGTCTGCAAC
 TCGACTCCATGAAGTCGGAATCGCTAGTAATCGTGGATCAGAATGCCACG

GTGAATACGTTCCCGGGCCTGTACACACCGCCCGTCACACCATGGGAGT
GGGTTGAAAAGAAGTAGGTAGCTAACCTCGGGAGGGCGCTTACCACT
TTGTGATTCATGACTGGGGTGAAGTCGTAACAAGGTAACCGTAGGGGAAC
CTGCGGTTGGATCACCTCCTTACCTTAAAGAAGCGTTCTTG

5

The match between the T1 sequence and the C1/C2 sequence is

AAAAAAATGCGCGGTCAAGAAAATTATTTAAATTTCCTCTGTCAGGCCGG
AATAACTCCCTATAATGCGCCACCACTGACACGGAACAAACGGCAAACACG
10 CCGCCGGGTCAAGCGGGTTCTCCTGAGAACTCCGGCAGAGAAAGCAAAA
ATAAATGCTTGACTCTGTAGCGGGAA

The match between the T2 sequence and the C1/C2 sequence is

15 TAAATTTCCTCTGTCAGGCCGGAAATAACTCCCTATAATGCGCCACCACTG
ACACGGAACAAACGGCAAACACGCCGCCGGTCAGCGGGTTCTCCTGAG
AACTCCGGCAGAGAAAGCAAAAATAATGCTTGACTCTGTAGCGGGAAAG
GCGTATTATGCACACCCCCGCGCCGCT

20 A C1/C2 short loop on chromosome 1 whose identifier is 3432 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene *btuB* and has the DNA sequence

25 TGCGCGGTCAAGAAAATTATTTAAATTTCCTCTGTCAGGCCGGAAATAACT
CCCTATAATGCGCCACCACTGACACGGAACAAACGGCAAACACGCCGCCGG
GTCAGCGGGTTCTCCTGAGAACTCCGGCAGAGAAAGCAAAAATAATG
CTTGACTCTGTAGCGGGAGGCGTATTATGCACACC...ACACCATGGGAGT
GGGTTGCAAAAGAAGTAGGTAGCTAACCTCGGGAGGGCGCTTACCACT
30 TTGTGATTCATGACTGGGGTGAAGTCGTAACAAGGTAACCGTAGGGGAAC
CTGCGGTTGGATCACCTCCTTACCTTAAAGAAGCGT

The match between the T1 sequence and the C1/C2 sequence is

TGCGCGGT CAGAAAATTATTTAAATT CCTCTT GTCAGGCCGAATAACT
CCCTATAATGCGCCACCACTGACACGGAACACGGCAAACACGCCGCCGG
GTCAGCGGGTTCTCCTGAGAACTCCGGCAGAGAAAGCAAAAATAATG
5 CTTGACTCTGTAGCGGGAA

The match between the T2 sequence and the C1/C2 sequence is

10 TAAATT CCTCTTGTCAGGCCGAATAACTCCCTATAATGCGCCACCACTG
ACACGGAACACGGCAAACACGCCGCCGGTCAGCGGGTTCTCCTGAG
AACTCCGGCAGAGAAAGCAAAAATAATGCTTAGCTCTGTAGCGGGAAAG
GCGTATTATGCACACCCCGCGCCGCT

15 A C1/C2 short loop on chromosome 1 whose identifier is 2218 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene clpB and has the DNA sequence

20 CTTGTCAGGCCGAATAACTCCCTATAATGCGCCACCACTGACACGGAAC
AACGGCAAACACGCCGCCGGC

The match between the T1 sequence and the C1/C2 sequence is

CTTGT CAGGCCGAATAACTCCCTATAATGCGCCACCACTGACACGGAAC
AACGGCAAACACGCCGCCGGC

25 The match between the T2 sequence and the C1/C2 sequence is

CTTGT CAGGCCGAATAACTCCCTATAATGCGCCACCACTGACACGGAAC
AACGGCAAACACGCCGCCGGC

30

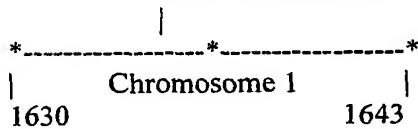
Example of a many-to-one connectron in archaea – M. jannaschii

In this example the existence of the T1-T2 (1630-1643) long loop is controlled by four C1/C2 short loops (1629, 1642, 124 and 1533).

5

1629 Chromosome 1
 1642 Chromosome 1
 124 Chromosome 1
 1533 Chromosome 1

10



15

A double stranded DNA loop of length 4.998 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 1630. This T1 control element has the DNA sequence

20

```
TTATTAATTAGTTCAAAGGATTTTATTAAATTCTAAGGGTTGCTGGTTT
GATTATTAGAACATTGAGTTATTGAATTATTCAAGATTAAAGATAAATTA
AGATTAATTAGGAAAGGAAATAAGATTCTCTAACAGACAAGTTAAATT
TTGGATTAAAAAGATAAAAAT
```

25

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 1643. This T2 control element has the DNA sequence

30

```
TTAATTCTAAGGGTAGCTGGTTGATTATTAGAACATTGAGTTATTG
AATTATTCAAGTTAAAGATAAGGATTAAATTAGGCAAGTAAATAAAAT
TTCTCTAACAAATAAGTTAAATTGGATTAAAAAGATAAAACTCT
GTTTTATTATGGAAAGAAAGAT
```

35

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

MJ1597 MJ1598 MJ1599 MJ1600 MJ1601 MJ1602

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2

5 short loops.

A C1/C2 short loop on chromosome 1 whose identifier is 1629 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene MJ1597 and has the DNA sequence

10

ATATGTTGAAATTGAAAATAAGAGTATTAGAAGTTATTAGTTCA
AAGGATTTTATTAAATTCTAAGGGTTGCTGGTTGATTATTAGAATAT
TTGAGTTATTGAATTATTCAAGATTTAAAAATTAA

15

The match between the T1 sequence and the C1/C2 sequence is

TTATTAAATTAGTCAAAGGATTTATTAAATTCTAAGGGTTGCTGGTT
GATTATTAGAATATTGAGTTATTGAATTATTCAAGATTTAAAAATTAA

20

The match between the T2 sequence and the C1/C2 sequence is

GCTGGTTGATTATTAGAATATTGAGTTATTGAATTATTCAAGATTTAA
AAAATTAA

25

A C1/C2 short loop on chromosome 1 whose identifier is 1642 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene MJ1602 and has the DNA sequence

30

ATTTAATTCTAACAAATAAGTTAAATTGGATTAAAAAGATAAAAATCT
TGAATTATTCAAGATTTAAAAATTAGGATTAATTAGGCAAGTAAATAAA
ATTTCTCTAACAAATAAGTTAAATTGGATTAAAAAGATAAAAATCT
CTGTTTATTATGGAAAGAAAGAT

The match between the T1 sequence and the C1/C2 sequence is

GCTGGTTGATTATTTAGAATATTCAGTTATTGAATTATTCAGATTTTA

5 AAAATTAA

The match between the T2 sequence and the C1/C2 sequence is

TTAATTCTAAGGGTTAGCTGGTTGATTATTTAGAATATTCAGTTATTG

10 AATTATTTCAGATTTAAAAATTAGGATTAATTAGGCAAGTAAATAAAAT
TTCTCTAACAAATAAGTTAAATTTGGATTAAAAAGATAAAAATACTCT
GTTTTATTATGGAAAGAAAGAT

15 A C1/C2 short loop on chromosome 1 whose identifier is 124 controls the expression
of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA
single strand that is 3'UTR to the gene MJ0112 and has the DNA sequence

ATTTAATTCTAAGGGTTGCTGGTTGATTATTTAGAATATTCAGTTATT
TGAATTATTTCAGATTTAAAAAT

20

The match between the T1 sequence and the C1/C2 sequence is

ATTTAATTCTAAGGGTTGCTGGTTGATTATTTAGAATATTCAGTTATT
TGAATTATTTCAGATTTAAAAAT

25

The match between the T2 sequence and the C1/C2 sequence is

GCTGGTTGATTATTTAGAATATTCAGTTATTGAATTATTCAGATTTTA
AAAAT

30

A C1/C2 short loop on chromosome 1 whose identifier is 1533 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene MJ1486 and has the DNA sequence

5 TTTTTATTAATTCTAAGGGTTGCTGGTTGATTATTTAGAATATTGAG
 TTTATT

The match between the T1 sequence and the C1/C2 sequence is

10 TTTTTATTAATTCTAAGGGTTGCTGGTTGATTATTTAGAATATTGAG
 TTTATT

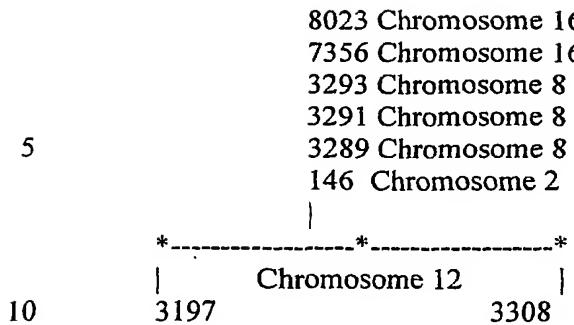
The match between the T2 sequence and the C1/C2 sequence is

15 GCTGGTTGATTATTTAGAATATTGAGTTTATT

Example of a many-to-one connectron in single-cell eukaryotes – *S. cerevisiae*

20 In this example the existence of the T1-T2 (5515-5533) long loop on chromosome 12 is controlled by seventeen C1/C2 short loops (5516, 5532, 1939, 2323, 1942, 3286, 3649, 4764, 4751, 5536, 6102, 8023, 7356, 3293, 3291, 3289 and 146).

25 5516 Chromosome 12
 5532 Chromosome 12
 1939 Chromosome 4
 2323 Chromosome 5
 1942 Chromosome 5
30 3286 Chromosome 7
 3649 Chromosome 8
 4764 Chromosome 12
 4751 Chromosome 12
 5536 Chromosome 13
35 6102 Chromosome 14



A double stranded DNA loop of length 6.466 kilo-bases on chromosome 12 is
15 bounded on the left by a T1 sequence whose identifier is 5515. This T1 control
element has the DNA sequence

20 AGGAAATTGTTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGGAATATGCCTTGTAGTAGTAGTAT
TTCACTGTTTGATTTAGTGTGTTGCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTG

This double stranded DNA loop is bounded on the right by a T2 control element
25 whose identifier is 5533. This T2 control element has the DNA sequence

30 ATTATGTATTGTGTAGTATAGTATATTGTAAGAAATTTTTCTAGGGA
ATATGCCTTGTAGTAGTAGTATTCACTGTTGATTTAGTGTGTTGC
ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAATC
TATAAAAGTAAACATAAAATAAGGTAGTAAGTAGCTTTGGTTGAACA
TCCGGGTAAGAGACAACAGGGCT

This long T1/T2 double stranded DNA loop modulates the expression of the
following genes

35

YLR467W

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

5 A C1/C2 short loop on chromosome 12 whose identifier is 5516 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YLR464W and has the DNA sequence

10 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGAAATATGCCTTGATGTAGTAGTAT
TTCACTGTTGATTTAGTGTGTCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTGGTTAACATCCGGTAAGAGAGACAACAGGGCT

15 A C1/C2 short loop on chromosome 12 whose identifier is 5532 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YLR467W and has the DNA sequence

20 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGAAATATGCCTTGATGTAGTAGTAT
TTCACTGTTGATTTAGTGTGTCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTGGTTAACATCCGGTAAGAGAGACAACAGGGCT

25

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

30 A C1/C2 short loop on chromosome 4 whose identifier is 1939 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed

as a RNA single strand that is 3'UTR to the gene YDR545W and has the DNA sequence

5 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTCTAGGGAAATATGCCTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGG

10 The match between the T1 sequence and the C1/C2 sequence is

AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTCTAGGGAAATATGCCTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGG

The match between the T2 sequence and the C1/C2 sequence is

20 ATTATGTATTGTGTAGTATAGTATATTGTAAGAAATTCTAGGGAA
ATATGCCTTGATGTAGTAGTATTCACTGTTGATTAGTGTGTTGC
ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAATC
TATAAAAGTAAACATAAAATAAGGTAGTAAGTAGCTTTGG

25 A C1/C2 short loop on chromosome 5 whose identifier is 2323 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YER189W and has the DNA sequence

30 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTCTAGGGAAATATGCCTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGACGGCAGTAGCGAGAGACAAGTG

GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTGAACATCCGGTAAGAGAGACAACAGGGCT

The match between the T1 sequence and the C1/C2 sequence is

5

AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGAAATATGCCTTGTAGTAGTAGTAT
TTCACTGTTGATTAGTGTGTCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA

10

AGGTAGTAAGTAGCTTTGGTTG

The match between the T2 sequence and the C1/C2 sequence is

15

ATTATGTATTGTGTAGTATAGTATTGTAAGAAATTTTTCTAGGGA
ATATGCCTTGTAGTAGTAGTATTCACTGTTGATTAGTGTGTTGTC
ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAATC
TATAAAAGTAAACATAAAATAAGGTAGTAAGTAGCTTTGGTTGAACA
TCCGGGTA
AGAGACAACAGGGCT

20

A C1/C2 short loop on chromosome 5 whose identifier is 1942 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YEL077C and has the DNA sequence

25

AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGAAATATGCCTTGTAGTAGTAGTAT
TTCACTGTTGATTAGTGTGTCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTGAACATCCGGTAAGAGAGACAACAGGGCT

The match between the T1 sequence and the C1/C2 sequence is

AGGAAATTGTTACGAAAGTCAGTATTGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGGAATATGCCTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGACGGCAGTAGCGAGAGACAAGTG
5 GGAAAGAGTAGGATAAAAAGACAATCTATAAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTG

The match between the T2 sequence and the C1/C2 sequence is

10 ATTATGTATTGTGTAGTATAGTATTGTAAGAAATTTTTCTAGGGA
ATATGCCTTGATGTAGTAGTATTCACTGTTGATTAGTGTGTTGC
ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAATC
TATAAAAAGTAAACATAAAATAAGGTAGTAAGTAGCTTTGGTTGAACA
TCCGGGTA
15 AGAGACAACAGGGCT

A C1/C2 short loop on chromosome 7 whose identifier is 3286 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YGR296W and has the DNA sequence
20

AGGAAATTGTTACGAAAGTCAGTATTGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGGAATATGCCTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGACGGCAGTAGCGAGAGACAAGTG
25 GGAAAGAGTAGGATAAAAAGACAATCTATAAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTAACATCCGGGTAAGAGACAACAGGGCT

The match between the T1 sequence and the C1/C2 sequence is

30 AGGAAATTGTTACGAAAGTCAGTATTGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGGAATATGCCTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGACGGCAGTAGCGAGAGACAAGTG

GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTG

The match between the T2 sequence and the C1/C2 sequence is

5

ATTATGTATTGTAGTATAGTATATTGTAAGAAATTTTTCTAGGGA
ATATGCCTTGTAGTAGTATTCACTGTTGATTAGTGTGTTGC
ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAGACAATC
TATAAAAGTAAACATAAAATAAGGTAGTAAGTAGCTTTGGTTGAACA
10 TCCGGGTAAGAGACAACAGGGCT

10

A C1/C2 short loop on chromosome 8 whose identifier is 3649 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YHR219W and has the DNA sequence

15

AGGAAATTGTTTACGAAAGTCAGTGATTATGTATTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGGAATATGCCTTGTAGTAGTAT
TTCACTGTTGATTAGTGTGTCACGGCAGTAGCGAGAGACAAGTG
20 GGAAAGAGTAGGATAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTGAACATCCGGGTAAGAGACAACAGGGCT

20

The match between the T1 sequence and the C1/C2 sequence is

25

AGGAAATTGTTTACGAAAGTCAGTGATTATGTATTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGGAATATGCCTTGTAGTAGTAT
TTCACTGTTGATTAGTGTGTCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTG

30

The match between the T2 sequence and the C1/C2 sequence is

ATTATGTATTGTAGTATAGTATATTGTAAGAAATTTTTCTAGGGA
ATATGCGTTTGATGTAGTAGTATTCACTGTTGATTAGTGGTTGC
ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAATC
TATAAAAAGTAAACATAAAATAAAGGTAGTAAGTAGCTTTGGTTGAACA
5 TCCGGGTAAGAGACAACAGGGCT

A C1/C2 short loop on chromosome 12 whose identifier is 4764 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YLL066C and has the DNA sequence
10

AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTAGTATAGTAT
ATTGTAAGAAATTCTAGGGAATATGCGTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGGTGCACGGCAGTAGCGAGAGACAAGTG
15 GGAAAGAGTAGGATAAAAAGACAATCTATAAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTAACATCCGGGTAAGAGACAACAGGGCT

The match between the T1 sequence and the C1/C2 sequence is

20 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTAGTATAGTAT
ATTGTAAGAAATTCTAGGGAATATGCGTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGGTGCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTG
25

The match between the T2 sequence and the C1/C2 sequence is

ATTATGTATTGTAGTATAGTATATTGTAAGAAATTTTTCTAGGGA
ATATGCGTTTGATGTAGTAGTATTCACTGTTGATTAGTGGTTGC
ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAATC
TATAAAAAGTAAACATAAAATAAAGGTAGTAAGTAGCTTTGGTTGAACA
30 TCCGGGTAAGAGACAACAGGGCT

A C1/C2 short loop on chromosome 12 whose identifier is 4751 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YLL067C and has the DNA sequence

5 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGGAATATGCCTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGACGGCAGTAGCGAGAGACAAGTG
10 GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTAACATCCGGTAAGAGACAACAGGGCT

The match between the T1 sequence and the C1/C2 sequence is

15 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGGAATATGCCTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA
20 AGGTAGTAAGTAGCTTTGGTT

The match between the T2 sequence and the C1/C2 sequence is

ATTATGTATTGTAGTATAGTATATTGTAAGAAATTTTTCTAGGGA
ATATGCCTTGATGTAGTAGTATTCACTGTTGATTAGTGTGTTGC
25 ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAATC
TATAAAAGTAAACATAAAATAAGGTAGTAAGTAGCTTTGGTTAAC
TCCGGGTAAGAGACAACAGGGCT

A C1/C2 short loop on chromosome 13 whose identifier is 5536 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YML133C and has the DNA sequence

AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGGAATATGCCTTGATGTAGTAGTAT
TTCACTGTTGATTTAGTGTGCACGGCAGTAGCGAGAGACAAGTG
5 GGAAAGAGTAGGATAAAAAGACAATCTATAAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTAACATCCGGTAAGAGACAAACAGGGCT

The match between the T1 sequence and the C1/C2 sequence is

10 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGGAATATGCCTTGATGTAGTAGTAT
TTCACTGTTGATTTAGTGTGCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTG

15

The match between the T2 sequence and the C1/C2 sequence is

ATTATGTATTGTGTAGTATAGTATATTGTAAGAAATTTTTCTAGGGA
ATATGCCTTGATGTAGTAGTATTCACTGTTGATTTAGTGTGTGC
20 ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAATC
TATAAAAAGTAAACATAAAATAAAGGTAGTAAGTAGCTTTGGTTAAC
TCCGGGTAAGAGACAAACAGGGCT

A C1/C2 short loop on chromosome 14 whose identifier is 6102 controls the
25 expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed
as a RNA single strand that is 3'UTR to the gene YNL339C and has the DNA
sequence

30 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGGAATATGCCTTGATGTAGTAGTAT
TTCACTGTTGATTTAGTGTGCACGGCAGTAGCGAGAGACAAGTG

GGAAAGAGTAGGATAAAAAGACAATCTATAAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTAACATCCGGGTAAAGAGACAAACAGGGCT

The match between the T1 sequence and the C1/C2 sequence is

5

AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGAAATATCGCTTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGTTGCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAAGTAAACATAAAATAA
10 AGGTAGTAAGTAGCTTTGGTTG

10

The match between the T2 sequence and the C1/C2 sequence is

15

ATTATGTTAGTAGTATAGTATATTGTAAGAAATTTTTCTAGGGA
ATATGCGTTGATGTAGTAGTATTCACTGTTGATTAGTGTGTTGC
ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAATC
TATAAAAAGTAAACATAAAATAAAGGTAGTAAGTAGCTTTGGTTAAC
TCCGGGTAAAGAGACAAACAGGGCT

20

A C1/C2 short loop on chromosome 16 whose identifier is 8023 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YPR204W and has the DNA sequence

25

AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGAAATATCGCTTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGTTGCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTAACATCCGGGTAAAGAGACAAACAGGGCT
30

30

The match between the T1 sequence and the C1/C2 sequence is

AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGAATATCGCTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGTTGCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAAGTAAACATAAAATAA
5 AGGTAGTAAGTAGCTTTGGTTG

The match between the T2 sequence and the C1/C2 sequence is

10 ATTATGTATTGTGTAGTATAGTATATTGTAAGAAATTTTTCTAGGGA
ATATCGCTTGATGTAGTAGTATTCACTGTTGATTAGTGTGTTGC
ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAATC
TATAAAAAGTAAACATAAAATAAGGTAGTAAGTAGCTTTGGTTGAACA
TCCGGGTAAGAGACAACAGGGCT

15 A C1/C2 short loop on chromosome 16 whose identifier is 7356 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YPL283C and has the DNA sequence

20 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGAATATCGCTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGTTGCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTGAACATCCGGGTAAGAGACAACAGGGCT
25

The match between the T1 sequence and the C1/C2 sequence is

30 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGAATATCGCTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGTTGCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTTGGTTG

The match between the T2 sequence and the C1/C2 sequence is

ATTATGTATTGTAGTATAGTATATTGTAAGAAATTTTTCTAGGGA
5 ATATGCGTTTGATGTAGTAGTATTCACTGTTGATTAGTGGTTGC
ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAATC
TATAAAAAGTAAACATAAAATAAGGTAGTAAGTAGCTTTGGTTGAACA
TCCGGGTAAGAGACAACAGGGCT

10 A C1/C2 short loop on chromosome 8 whose identifier is 3293 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YHL050C and has the DNA sequence

15 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGGAATATGCGTTT

The match between the T1 sequence and the C1/C2 sequence is

20 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTAGTATAGTAT
ATTGTAAGAAATTTTTCTAGGGAATATGCGTTT

The match between the T2 sequence and the C1/C2 sequence is

25 ATTATGTATTGTAGTATAGTATATTGTAAGAAATTTTTCTAGGGA
ATATGCGTTT

30 A C1/C2 short loop on chromosome 8 whose identifier is 3291 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YHL050C and has the DNA sequence

ATGTAGTAGTATTCACTGTTGATTAGTGTTCACGGCAGTAGC
GAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAA

The match between the T1 sequence and the C1/C2 sequence is

5

ATGTAGTAGTATTCACTGTTGATTAGTGTTCACGGCAGTAGC
GAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAA

The match between the T2 sequence and the C1/C2 sequence is

10

ATGTAGTAGTATTCACTGTTGATTAGTGTTCACGGCAGTAGC
GAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAA

A C1/C2 short loop on chromosome 2 whose identifier is 145 controls the expression
15 of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA
single strand that is 3'UTR to the gene YBL113C and has the DNA sequence

CTATAAAAAGTAAACATAAAATAAAGGTAGTAAGTAGCTTTGGTTGAAC
ATCCGGGTAAGAGACAAACAGGCT

20

The match between the T1 sequence and the C1/C2 sequence is

CTATAAAAAGTAAACATAAAATAAAGGTAGTAAGTAGCTTTGGTTG

25

The match between the T2 sequence and the C1/C2 sequence is

CTATAAAAAGTAAACATAAAATAAAGGTAGTAAGTAGCTTTGGTTGAAC
ATCCGGGTAAGAGACAAACAGGCT

30

A C1/C2 short loop on chromosome 8 whose identifier is 3289 controls the
expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed

as a RNA single strand that is 3'UTR to the gene YHL050C and has the DNA sequence

CTATAAAAAGTAAACATAAAATAAAGGTAGTAAGTAGCTTTGGTTGAAC
5 ATCCGGGTAAGAGACAAACAGGCT

The match between the T1 sequence and the C1/C2 sequence is

CTATAAAAAGTAAACATAAAATAAAGGTAGTAAGTAGCTTTGGTTG

10

The match between the T2 sequence and the C1/C2 sequence is

CTATAAAAAGTAAACATAAAATAAAGGTAGTAAGTAGCTTTGGTTGAAC
15 ATCCGGGTAAGAGACAAACAGGCT

15

A C1/C2 short loop on chromosome 2 whose identifier is 146 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YBL113C and has the DNA sequence

20

AGGAAATTGTTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAA

The match between the T1 sequence and the C1/C2 sequence is

25

AGGAAATTGTTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAA

The match between the T2 sequence and the C1/C2 sequence is

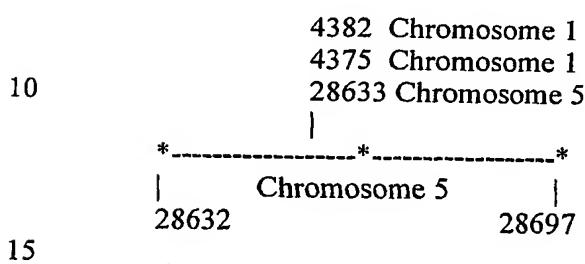
30

ATTATGTATTGTGTAGTATAGTATATTGTAAGAAA

Example of a many-to-one connectron in multi-cell eukaryotes – C. elegans

In this example the existence of the T1-T2 (3197-3308) long loop on chromosome 5

5 is controlled by three C1/C2 short loops (4382, 4375 and 28633).



A double stranded DNA loop of length 58.451 kilo-bases on chromosome 5 is bounded on the left by a T1 sequence whose identifier is 28632. This T1 control element has the DNA sequence

20

GCAAAAATTGACTGAAAATTGAATTCCCGCAAAAAATTGACTGAAAAT
TTGAATTCCGCCAAAAATTGACTGAAAATTGAA

25 This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 28697. This T2 control element has the DNA sequence

30

CAAAAAATTGACTGAAAATTGAATTCCCTCCAAAAATTGACTGAAAAT
TTGAATTCCGCCAAAAATTGACTGAAAATTGAATATCCGCCAAAAA
TTGACTGAAAATTGAATTCCCGCCGAAAATTAAATGAAAAATGGAATT
TCTCGCCGAA

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

35

M162.8 M162.4 M162.3 M162.6 M162.2 M162.1 M162.7

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

5

A C1/C2 short loop on chromosome 1 whose identifier is 4382 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene Y43F8B.10 and has the DNA sequence

10

ATTATAGAAAATTAAATTCCCTCCAAAAAATTGACTGAAAATTGAATT
TCCCTCCAAAAATTGACTGAAAATTGAATTCCCGCCAAAAATTGACTG
AAAATTGAATATCCCGCCAAAAATTGACTGAAAATTGAATTCCCGCC
GAAAATTAAATGAAAAATGGAATTCTCGCCGAAAAATTCACTAAAAATT
15 TGAATTCCCTGCCAAAAATTGACTGAAAATTGAATTCTTGCCAAAAAA
GTGACTGGAAATTGAATTCCCTCCAAAAATTGACTGAAATTGAATT
CCCGCTAAAAGTTGACT

The match between the T1 sequence and the C1/C2 sequence is

20

CAAAAATTGACTGAAAATTGAATTCCCGC

The match between the T2 sequence and the C1/C2 sequence is

25

CAAAAATTGACTGAAAATTGAATTCCCTCCAAAAATTGACTGAAAAT
TTGAATTCCCGCCAAAAATTGACTGAAAATTGAATATCCCGCCAAAAA
TTGACTGAAAATTGAATTCCCGCCGAAAATTAAATGAAAAATGGAATT
TCTCGCCGAA

30

A C1/C2 short loop on chromosome 1 whose identifier is 4375 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed

as a RNA single strand that is 3'UTR to the gene Y43F8B.10 and has the DNA sequence

5 ATTATAGAAAATTAAATTCCCTCCAAAAAATTGACTGAAAATTGAATT
TCCCTCCAAAAATTGACTGAAAATTGAATTCCCGCCAAAAATTGACTG
AAAATTGAATATCCCGCCAAAAATTGACTGAAAATTGAATTCCCGCC
GAAAATTAAATGAAAATGGAATTCTCGCCGAAAAATTCACTAAAAATT
TGAATTCTGCCAAAAATTGACTGAAAATTGAATTCTGCCAAAAA
10 GTGACTGGAAATTGAATTCCCTCCAAAAATTGACTGAAATTGAAATT
CCCGCTAAAAGTTGACT

The match between the T1 sequence and the C1/C2 sequence is

15 CAAAAATTGACTGAAAATTGAATTCCCGC
The match between the T2 sequence and the C1/C2 sequence is

20 CAAAAAATTGACTGAAAATTGAATTCCCTCCAAAAATTGACTGAAAAT
TTGAATTCCGCCAAAAATTGACTGAAAATTGAATATCCCGCCAAAAA
TTGACTGAAAATTGAATTCCCGCCGAAAATTAAATGAAAATGGAATT
TCTCGCCGAA

25 A C1/C2 short loop on chromosome 5 whose identifier is 28633 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene M162.5 and has the DNA sequence

CAAAAATTGACTGAAAATTGAATTCCCGCAAAAAATTGACTGAAAATT
TGAATTCCGCCAAAAATTGACTGAAAATTGAA

30 The match between the T1 sequence and the C1/C2 sequence is

CAAAAATTGACTGAAAATTGAATTCCCGCAAAAAATTGACTGAAAATT
TGAATTCCCGCCAAAAATTGACTGAAAATTGAA

The match between the T2 sequence and the C1/C2 sequence is

5

CAAAAATTGACTGAAAATTGAATTCCC

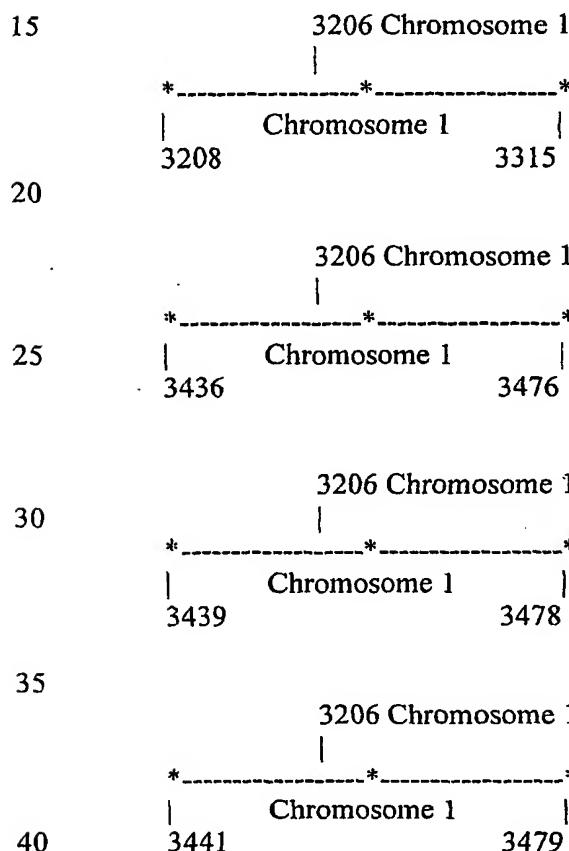
10

3. One connectron controls the expression of many sets of genes in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes.

5 One C1/C2 short loop can control the existence of a many T1-T2 long loops. The C1/C2 short loop can be on the same chromosome or on different chromosomes from the T1-T2 long loops. This relationship is described as "one-to-many". This relationship exists in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes.

10 Example of a one-to-many connectron in prokaryotes – E. coli

In this example the existence of T1-T2 (3208-3315, 3436-3476, 3439-3478 and 3441-3479) long loops are controlled by one C1/C2 short loop (3206).



5 A double stranded DNA loop of length 93.377 kilo-bases on chromosome 1 is
 bounded on the left by a T1 sequence whose identifier is 3208. This T1 control
 element has the DNA sequence

ACTCATCTCGGGTGATGTTGAGATATTGCTCTTAAAAATCTGGATCA
 AGCTGAAAATTGAAACACTGAACACAACGAAAGTTGTCGTGAGTCTCTCAA
 10 ATTTTCGCAACACGATGATGAATCGAAAGAACATCTCGGGTTGTGAGG
 TTAAGCGACTAAGCGTACACGGTGGATGCCCTGGC...AGTGTGTTCGACA
 CACTATCATTAACTGAATCCATAGGTTAATGAGGCGAACCGGGGGAACTG
 AAACATCTAAGTACCCCGAGGAAAAGAAATCAACCGAGATTCCCCCAGTA
 GCGGCGAGCGAACGGGGAGCAGCCCAGAGCCTGAATCAGT

15
 This double stranded DNA loop is bounded on the right by a T2 control element
 whose identifier is 3315. This T2 control element has the DNA sequence

20 TTTGCTCTTAAAAATCTGGATCAAGCTGAAAATTGAAACACTGAACAAAC
 GAAAGTTGTCGTGAGTCTCTCAAATTTGCAACTCTGAAGTGAAACACATC
 TTCGGGTTGTGAGGTTAAGCGACTAAGCGTACACGGTGGATGCCCTGGCA
 GTCAGAGGCGATGAAGGACGTGCTAATCTGCGATA...GGTTAATGAGGCG
 AACCGGGGGAACTGAAACATCTAAGTACCCCGAGGAAAAGAAATCAACC
 GAGATTCCCCCAGTAGCGGCGAGCGAACGGGGAGCAGCCCAGAGCCTGA
 25 ATCAGTGTGTGTTAGTGGAAAGCGTCTGGAAA

This long T1/T2 double stranded DNA loop modulates the expression of the
 following genes

30	rriC	rrfC	aspT	trpT	yifA	yifE	yifB	ilvL	ilvG_1
	ilvM	ilvE	ilvD	ilvA	ilvY	ilvC	ppiC	b3776	rep
	gppA	rhlB	trxA	rhoL	rho	rfe	wzzE	wecB	rffH

wecD	wecE	wzxE	yifM_2	wecG	yifK	argX	hisR
leuT	proM	aslB	aslA	hemY	hemX	hemD	cyaA
cyaY	b3808	dapF	uvrD	b3814	corA	yigF	yigG
yigI	pldA	recQ	yigJ	yigK	pldB	yigL	yigM
5	metE	ysgA	udp	yigN	ubiE	yigP	b3836
metE	ysgA	udp	yigN	ubiE	yigP	b3836	yigU
yigW_1	rfaH	yigC	ubiB	fadA	fadB	pepQ	trkH
hemG	rrsA	ileT					

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2

10 short loops.

A C1/C2 short loop on chromosome 1 whose identifier is 3206 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene rrsC and has the DNA sequence

15

GTCCCCTTCGTCTAGAGGCCAGGACACCGCCCTTCACGGCGGTAAACAG
 GGGTTCGAATCCCCTAGGGGACGCCACTTGCTGGTTGTGAGTGAAAGTC
 ACCTGCCTTAATATCTCAAAACTCATCTCGGGTGATGTTGAGATATTG
 CTCTTTAAAATCTGGATCAAGCTGAAAATTGAAA...ACCGGCGATTCCG
 20 AATGGGGAAACCCAGTGTGTTGACACACTATCATTAACTGAATCCATA
 GGTTAATGAGGCGAACCGGGGAACTGAAACATCTAAGTACCCGAGGA
 AAAGAAATCAACCGAGATTCCCCAGTAGCGCGAGCGAACGGGGAGCA
 GCCCAGAGCCTGAATCAGT

25

The match between the T1 sequence and the C1/C2 sequence is

ACTCATCTCGGGTGATGTTGAGATATTGCTCTTAAAATCTGGATCA
 AGCTGAAAATTGAAACACTGAACAAACGAAAGTTGTTCGTGAGTCTCTCAA
 ATTTTCGCAACACGATGATGAATCGAAAGAAACATCTCGGGTTGTGAGG
 30 TTAAGCGACTAAGCGTACACGGTGGATGCCCTGGC...AGTGTGTTCGACA
 CACTATCATTAACTGAATCCATAGGTTAATGAGGCGAACCGGGGGAACTG

AAACATCTAAGTACCCCGAGGAAAAGAAATCAACCGAGATTCCCCCAGTA
GCGGCGAGCGAACGGGGAGCAGCCCAGAGCCTGAATCAGT

The match between the T2 sequence and the C1/C2 sequence is

5

TTTGCTTTAAAAATCTGGATCAAGCTGAAAATTGAAACACTGAACAAC
GAAAGTTGTCGTGAGTCTCTCAAATTCGCAAC

10

A double stranded DNA loop of length 41.279 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 3436. This T1 control element has the DNA sequence

15

ACGCAACCGGTGATAAGCAATTCGTGCCCCCTCGTAGAGGCCAG
GACACCGCCCTTCACGGCGGTAAACAGGGGTTCGAATCCCCTAGGGGACG
CCACTTGCTGGTT

20

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 3476. This T2 control element has the DNA sequence

AGTAAAAAGCAAGGCGTCTGCGAAGCAGACTGATACGTCCCCCTCGTCT
AGAGGCCAGGACACCGCCCTTCACGGCGGTAAACAGGGGTTCGAATCCC
CTAGGGGACGCCACTTGCTGGTTGTGAGTGAAAGTCACCTGCCTTAATA

25

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

	gltT	rriB	rrfB	murB	coaA	b3975	tyrU	thrT	tufB
30	secE	nusG	rplK	rplA	rplJ	rplL	rpoB	rpoC	htrC
	thiH	thiF	thiE	yjaE	yjaD	hemE	nfi	yjaG	hupA
	yjaH	yjaI	hydH	purD	purH				

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

5 A C1/C2 short loop on chromosome 1 whose identifier is 3206 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene rrsC and has the DNA sequence

10 GTCCCCCTCGTCTAGAGGCCAGGACACCGCCTTCACGGCGGTAAACAG
GGGTTCGAATCCCTAGGGGACGCCACTTGCTGGTTGTGAGTGAAGTC
ACCTGCCTTAATATCTCAAAACTCATCTCGGGTGATGTTGAGATATTG
CTCTTTAAAAATCTGGATCAAGCTGAAAATTGAAACACTGAACAACGAAA
GTTGTTCGTGAGTCTCTCAAATTTCGCAACACGATGATGAATCGAAAGA
AACATCTCGGGTTGTGAGGTTAAGCGACTAACCGTACACGGTGGATGCC
15 CTGGCAGTCAGAGGCGATGAAGGACGTGCTAATCTGCGATAAGCGTCGGT
AAGGTGATATGAACCGTTATAACCGCGATTCCGAATGGGAAACCCAG
TGTGTTCGACACACTATCATTAACTGAATCCATAGGTTAATGAGGCGAA
CCGGGGGAACTGAAACATCTAAGTACCCCGAGGAAAAGAAATCAACCGA
GATTCCCCCAGTAGCGGGGAGCGAACGGGGAGCAGCCCAGAGCCTGAAT
20 CAGT

The match between the T1 sequence and the C1/C2 sequence is

25 GTCCCCCTCGTCTAGAGGCCAGGACACCGCCTTCACGGCGGTAAACAG
GGGTTCGAATCCCTAGGGGACGCCACTTGCTGGTT

The match between the T2 sequence and the C1/C2 sequence is

30 GTCCCCCTCGTCTAGAGGCCAGGACACCGCCTTCACGGCGGTAAACAG
GGGTTCGAATCCCTAGGGGACGCCACTTGCTGGTTGTGAGTGAAGTC
ACCTGCCTTAATA

5

A double stranded DNA loop of length 41.336 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 3439. This T1 control element has the DNA sequence

CCTTAATATCTCAAAACTCATCTCGGGTGATGTTGAGATATTGCTCTT
AAAAATCTGGATCAAGCTGAAAATTGAAACACTGAACACAACGA

10

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 3478. This T2 control element has the DNA sequence

GTGATGTTGAGATATTGCTCTTAAAAATCTGGATCAAGCTGAAAATTG
AAACACTGAACAAACGAAAGTTGTCGTGAGTCTCTCAAATT

15

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

20

rrfB	rrfB	murB	coaA	b3975	tyrU	thrT	tufB	secE
nusG	rplK	rplA	rplJ	rplL	rpoB	rpoC	htrC	thiH
thiF	thiE	yjaE	yjaD	hemE	nfi	yjaG	hupA	yjaH
yjaI	hydH	purD	purH	gltV				

25

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

30

A C1/C2 short loop on chromosome 1 whose identifier is 3206 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene rsC and has the DNA sequence

GTCCCCTTCGTCTAGAGGCCAGGACACCGCCCTTCACGGCGGTAAACAG
GGGTTCGAACATCCCTAGGGGACGCCACTGCTGGTTGTGAGTGAAAGTC

ACCTGCCTTAATATCTCAAAACTCATCTCGGGTGTGAGATATTG
CTCTTTAAAAATCTGGATCAAGCTGAAAATTGAAA...ACCGCGATTCCG
AATGGGGAAACCCAGTGTGTTCGACACACTATCATTAACTGAATCCATA
GGTTAACGAGGCGAACCGGGGGAACTGAAACATCTAAGTACCCCGAGGA
AAAGAAATCAACCGAGATTCCCCAGTAGCGGCGAGCGAACGGGGAGCA
GCCAGAGCCTGAATCAGT

The match between the T1 sequence and the C1/C2 sequence is

10 CCTTAATATCTCAAAACTCATCTCGGGTGTGAGATATTGCTCTTT
AAAAATCTGGATCAAGCTGAAAATTGAAACACTGAACAAACGA

The match between the T2 sequence and the C1/C2 sequence is

15 GTGATGTTGAGATATTGCTCTTAAAAATCTGGATCAAGCTGAAAATTG
AAACACTGAACAACGAAAGTTGTCGTGAGTCTCTCAAATTT

20 A double stranded DNA loop of length 38.285 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 3441. This T1 control element has the DNA sequence

25 AATTTCGAACACGATGATGAATCGAAAGAAACATCTCGGGTTGTGAG
GTTAAGCGACTAACCGTACACGGTGGATGCCCTGGCAGTCAGAGGCGATG
AAGGACGTGCTAATCTCGATAAGCGTGGTAAGGTGATATGAACCGTTA
TAACCGGCATTCCGAATGGGGAAACCCAGTGTGT...GATGAGAGAAGA
TTTCAGCCTGATACAGATTAAATCAGAACGAGAAGCGGTCTGATAAAA
CAGAATTGCTGGCGGCAGTAGCGCGGTGGTCCCACCTGACCCCATGCC
30 GAACTCAGAAGTGAAACGCCGTAGCGCCGATGGTAGTGTGGGTCTCCCC
ATGCGAG

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 3479. This T2 control element has the DNA sequence

5 AAGAAACATCTCGGGTTGTGAGGTTAACGCACTAACGCGTACACGGTGGA
 TGCCTGGCAGTCAGAGGCGATGAAGGACGTGCTAATCTGCGATAAGCGT
 CGGTAAGGTGATATGAACCGTTATAACCGCGATTCCGAATGGGGAAAC
 CCAGTGTGTTCGACACACTATCATTAACCTGAATCC..CAGATTAAATCAG
 AACGCAGAAGCGGTCTGATAAAACAGAATTGCCTGGCGGCAGTAGCGC
 GGTGGTCCCACCTGACCCATGCCGAACTCAGAAGTGAAACGCCGTAGCG
 10 CCGATGGTAGTGTGGGTCTCCCCATGCGAGAGTAGGAACTGCCAGGCA
 TCAAATTA

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

15 rrlB rrfB murB coaA b3975 tyrU thrT tufB secE
 nusG rplK rplA rplJ rplL rpoB rpoC htrC thiH
 thiF thiE yjaE yjaD hemE nfi yjaG hupA yjaH
 yjaI hydH purD purH gltV

20 The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

25 A C1/C2 short loop on chromosome 1 whose identifier is 3206 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene rrsC and has the DNA sequence

30 GTCCCCTCGTCTAGAGGCCAGGACACCGCCTTCACGGCGGTAAACAG
 GGGTTCGAATCCCTAGGGGACGCCACTGCTGGTTGTGAGTGAAAGTC
 ACCTGCCTTAATATCTCAAAACTCATCTCGGGTGTGAGATATTG
 CTCTTAAAAATCTGGATCAAGCTGAAAATTGAAA...ACCGCGATTCCG
 AATGGGGAAACCCAGTGTGTTCGACACACTATCATTAACCTGAATCCATA

GGTTAATGAGGCCAACCGGGGAACTGAAACATCTAAGTACCCCGAGGA
AAAGAAATCAACCGAGATTCCCCAGTAGCGCGAGCGAACGGGGAGCA
GCCAGAGCCTGAATCAGT

5 The match between the T1 sequence and the C1/C2 sequence is

AATTTCGAACACGATGATGAATCGAAAGAAACATCTCGGGTTGTGAG
GTTAAGCGACTAACCGTACACGGTGGATGCCCTGGCAGTCAGAGGCGATG
AAGGACGTGCTAATCTGCGATAAGCGTCGGTAAGGTGATATGAACCGTTA
10 TAACC CGCGATTCCGAATGGGAAACCCAGTGTGTTCGACACACTATC
ATTA ACTGAATCCATAGGTTAATGAGGCGAACCGGGGAACTGAAACATC
TAAGTACCCCGAGGAAAAGAAATCAACCGAGATTCCCCAGTAGCGCG
AGCGAACGGGAGCAGCCCAGAGCCTGAATCAGT

15 The match between the T2 sequence and the C1/C2 sequence is

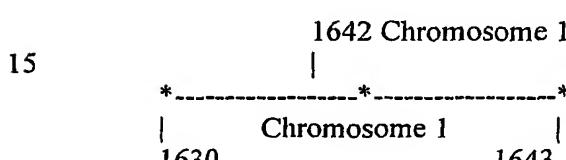
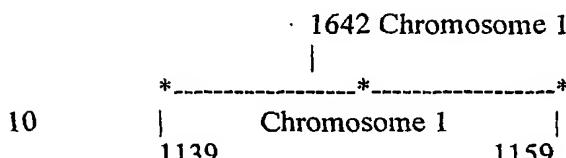
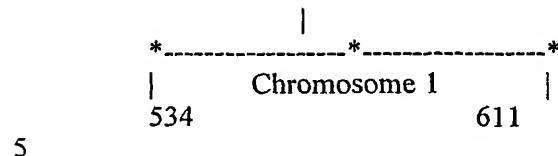
AAGAAACATCTCGGGTTGTGAGGTTAACCGACTAACCGTACACGGTGGA
TGCCCTGGCAGTCAGAGGCGATGAAGGACGTGCTAATCTGCGATAAGCGT
CGGTAAAGGTGATATGAACCGTTATAACCGCGATTCCGAATGGGAAAC
20 CCAGTGTGTTCGACACACTATCATTA ACTGAATCCATAGGTTAATGAGGC
GAACCGGGGAACTGAAACATCTAAGTACCCCGAGGAAAAGAAATCAAC
CGAGATTCCCCAGTAGCGCGAGCGAACGGGGAGCAGCCCAGAGCCTG
AATCAGT

25 -----

Example of a one-to-many connectron in archaea – M. jannaschii

In this example the existence of T1-T2 (534-611, 1139-1159, and 1630-1643) long
30 loops are controlled by one C1/C2 short loop (1642).

1642 Chromosome 1



20

A double stranded DNA loop of length 72.886 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 534. This T1 control element has the DNA sequence

25

TAAGTAAATAAAATTCTCTAACAAATAAGTTAAATTGGATTAAAAAGATA

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 611. This T2 control element has the DNA sequence

30

TAAATAAAATTCTCTAACAAATAAGTTAAATTGGATTAAAAAGATA
AAAATGCT

35

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

MJ0486	MJ0487	MJ0488	MJ0489	MJ0490	MJ0492	MJ0493
MJ0494	MJ0495	MJ0496	MJ0497	MJ0499	MJ0500	MJ0501

MJ0502	MJ0503	MJ0504	MJ0506	MJ0507	MJ0508	MJ0509	
MJ0510	MJ0511	MJ0512	MJ0513	MJ0514	MJ0514	MJ0517	
MJ0519	MJ0520	MJ0521	MJ0522	MJ0523	MJ0525	MJ0526	
MJ0526	MJ0529	MJ0530	MJ0531	MJ0532	MJ0534	MJ0535	
5	MJ0536	MJ0538	MJ0539	MJ0540	MJ0541	MJ0542	MJ0543
MJ0544	MJ0545	MJ0547	MJ0548	MJ0549	MJ0550	MJ0552	
MJ0553	MJ0554	MJ0555	MJ0556	MJ0558	MJ0559	MJ0560	
MJ0561	MJ0562	MJ0563	MJ0564				

10 The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

15 A C1/C2 short loop on chromosome 1 whose identifier is 1642 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene MJ1602 and has the DNA sequence

20 ATTTAATTCTAACGGTTAGCTGGTTGATTATTTAGAAATATTGAGTTAT
TGAATTATTCAGATTTAAAAATTAGGATTAATTAGGCAAGTAAATAAA
ATTTCTCTAACAAATAAGTTAAATTTTGATTTAAAAAGATAAAAATACT
CTGTTTATTATGGAAAGAAAGAT

The match between the T1 sequence and the C1/C2 sequence is

AAGTAAATAAAATTCTAACAAATAAGTTAAATT

25 The match between the T2 sequence and the C1/C2 sequence is

TAAATAAAATTCTAACAAATAAGTTAAATTTTGATTTAAAAAGATA
AAAAT

30 -----

A double stranded DNA loop of length 14.509 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 1139. This T1 control element has the DNA sequence

5 ATTTATTAATTAGTCAAAGGATTTATTAATTCTAAGGGTAGCTGG
 TTTGATTGTTAAAATATTGAGTTA

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 1159. This T2 control element has the DNA sequence

10 ATTTAATTCTAAGGGTAGCTGGTTGATTATTAGAATATTGAGTTAT
 TGAATTATTCAGATTTAAAAATTA

This long T1/T2 double stranded DNA loop modulates the expression of the
15 following genes

MJ1096 MJ1097 tRNA-Arg-3 MJ1098 MJ1099 MJ1100 MJ1101
MJ1102 MJ1103 MJ1104 MJ1105 MJ1106 MJ1107 MJ1108

20 The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

A C1/C2 short loop on chromosome 1 whose identifier is 1642 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed
25 as a RNA single strand that is 3'UTR to the gene MJ1602 and has the DNA sequence

ATTTAATTCTAAGGGTAGCTGGTTGATTATTAGAATATTGAGTTAT
TGAATTATTCAGATTTAAAAATTAGGATTAATTAGGCAAGTAAATAAA
ATTTCTCTAACAAATAAGTTAAATTGGATTAAAAAGATAAAAATACT
30 CTGTTTATTATGGAAAGAAAGAT

The match between the T1 sequence and the C1/C2 sequence is

ATTTAATTCTAAGGGTAGCTGGTTGATT

The match between the T2 sequence and the C1/C2 sequence is

5

ATTTAATTCTAAGGGTAGCTGGTTGATTATTAGAATATTGAGTTAT
TGAATTATTCAGATTTAAAAATTA

10

A double stranded DNA loop of length 4.998 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 1630. This T1 control element has the DNA sequence

15

TTATAATTAGTCAAAGGATTTATTAAATTCTAAGGGTTGCTGGTT
GATTATTAGAATATTGAGTTATTGAATTATTCAGATTTAAAAATTA
AGATTAATTAGGAAAGGAAATAAGATTCTCTAACAGACAAGTAAATT
TTGGATTAAAAAGATAAAAAT

20

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 1643. This T2 control element has the DNA sequence

TTAATTCTAAGGGTAGCTGGTTGATTATTAGAATATTGAGTTATTG
AATTATTCAGATTTAAAAATTAGGATTAATTAGGCAAGTAAATAAAAT
25 TTCTCTAACAAATAAGTAAATTGGATTAAAAAGATAAAAATCT
GTTTATTATGGAAAGAAAGAT

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

30

MJ1597 MJ1598 MJ1599 MJ1600 MJ1601 MJ1602

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

5 A C1/C2 short loop on chromosome 1 whose identifier is 1642 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene MJ1602 and has the DNA sequence

10 ATTTAATTCTAAGGGTAGCTGGTTGATTATTTAGAATATTGAGTTAT
TGAATTATTCAAGATTTAAAAATTAGGATTAATTAGGCAAGTAAATAAA
ATTCTCTAACAAATAAGTTAAATTTGGATTAAAAAGATAAAAATACT
CTGTTTATTATGGAAAGAAAGAT

The match between the T1 sequence and the C1/C2 sequence is

15 GCTGGTTGATTATTTAGAATATTGAGTTATTGAATTATTCAAGATTTA
AAAATTA

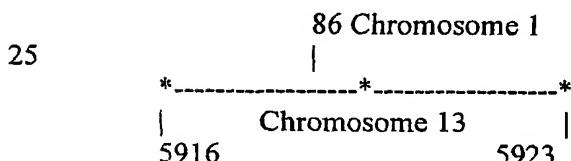
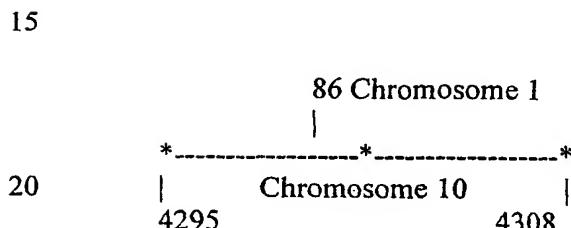
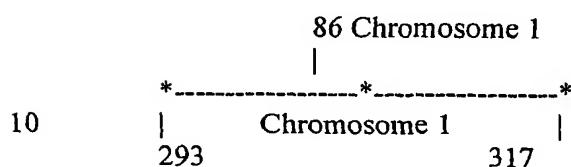
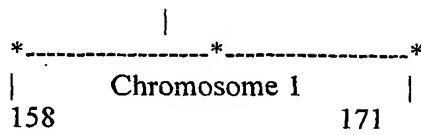
The match between the T2 sequence and the C1/C2 sequence is

20 TTAATTCTAAGGGTAGCTGGTTGATTATTTAGAATATTGAGTTATTG
AATTATTCAAGATTTAAAAATTAGGATTAATTAGGCAAGTAAATAAAAT
TTCTCTAACAAATAAGTTAAATTTGGATTAAAAAGATAAAAATACTCT
GTTTTATTATGGAAAGAAAGAT

25 -----

Example of a one-to-many connectron in single-cell eukaryotes – *S. cerevisiae*

30 In this example the existence of T1-T2 (158-171, 293-317, 4295-4308 and 5916-
5923) long loops are controlled by one C1/C2 short loop (86).



25

A double stranded DNA loop of length 20.391 kilo-bases on chromosome 2 is bounded on the left by a T1 sequence whose identifier is 158. This T1 control element has the DNA sequence

35

CCAATTGTTGGAATAAAATCAACTATCATCTACTAACTAGTATTACGTT
ACTAGTATATTATCATATACGGTGTAGAAGATGACGCAAATGATGAGAA
ATAGTCATCTAAATTAGTGGAGCTGAAACGCAAGGATTGATAATGTAAT
AG

40

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 171. This T2 control element has the DNA sequence

5 ATAATTGTTGGAATAAAATCAACTATCATCTACTAAGTATTACGTT
ACTAGTATATTATCATATACGGTGTAGAACAGATGACACAAATGATGAGAA
ATAGTCATCTAAATTAGTGGAAAGCTGAAACGCAAGGATTGATAATGTAAT
AGGATCAATGAATATTAACATATAAAATGATGATAATAATA

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

10 YBL107W-A TL(UAA)B1 YBL107C YBL106C YBL105C YBL104C
YBL103C YBL102W YBL101C

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

15 A C1/C2 short loop on chromosome 1 whose identifier is 86 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YAR009C and has the DNA sequence

20 ATCTATTACATTATGGGTGGTATGTTGGAATAGAAATCAACTATCATCTAC
TAACTAGTATTACATTACTAGTATATTATCATATACGGTGTAGAACAGATG
ACGCAAATGATGAGAAATAGTCATCTAAATTAGTGGAAAGCTGAAACGCA
AGGATTGATAATGTAATAGGATCAATGAATATAAACATATAAAACGGAAT
GAGGAATAATCGTAATATTAGTATGTAGAAATATAGATTCCATTGAGG
25 ATTCCCTATATCCTCGAGGAGAACTTCTAGTATATTCTGTATACCTAACATT
ATAGCCTTATCAACAATGGAATCCAACAAATTATCTCAACATTACCCAT
TTCTCAGAA

30 The match between the T1 sequence and the C1/C2 sequence is
AAATCAACTATCATCTACTAAGTATTAC

The match between the T2 sequence and the C1/C2 sequence is

AAATCAACTATCATCTACTAACTAGTATTAC

5

A double stranded DNA loop of length 38.470 kilo-bases on chromosome 2 is bounded on the left by a T1 sequence whose identifier is 293. This T1 control element has the DNA sequence

10

GAATTGTTGGAATAAAATCCACTATCGTCTATCAACTAATAGTTATTA
TCAATATATTATCATATACGGTGTAAAGATGATGACATAAGTTATGAGAA
GCTGTCATCGAACGTTAGAGGAAGCTGAAGTGCAAGGATTGATAATGTAAT
AGGATAATGAAACATATAAACCGGAATGAGGAATAATCGTAATATTAGT
15 ATGTAGAAATATAGATTCCATTTGAGGATTCTATATCCTTGAGGAGAAC
TTCTAGT

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 317. This T2 control element has the DNA sequence

20

AATATTAGTATGTAGAAATATAGATTCCATTTGAGGATTCTATATCCTC
GAGGAGAACTTCTAGTATATTCTGTA

25

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

YBL005W-B TS(AGA)B YBL004W YBL003C YBL002W YBL001C
YBR001C YBR002C YBR003W YBR004C YBR005W YBR006W
YBR007C YBR008C YBR009C YBR010W YBR011C YBR012C

30

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

A C1/C2 short loop on chromosome 1 whose identifier is 86 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YAR009C and has the DNA sequence

5

ATCTATTACATTATGGGTGGTATGTTGGAATAGAAATCAACTATCATCTAC
TAACTAGTATTACATTACTAGTATATTATCATATACGGTGTTAGAAGATG
ACGCAAATGATGAGAAATAGTCATCTAAATTAGTGGAAAGCTGAAACGCA
AGGATTGATAATGTAATAGGATCAATGAATATAAACATATAAAACGGAAT
GAGGAATAATCGTAATATTAGTATGTAGAAATATAGATTCCATTTGAGG
10 ATTCCTATATCCTCGAGGAGAACTTCTAGTATATTCTGTATACCTAATATT
ATAGCCTTATCAACAATGGAATCCCAACAATTATCTCAACATTACCCAT
TTCTCAGAA

10

15

The match between the T1 sequence and the C1/C2 sequence is

AAACATATAAAACGGAATGAGGAATAATCGTAATATTAGTATGTAGAAAT
ATAGATTCCATTTGAGGATTCTATATCCT

20

The match between the T2 sequence and the C1/C2 sequence is

AATATTAGTATGTAGAAATATAGATTCCATTTGAGGATTCTATATCCTC
GAGGAGAACTTCTAGTATATTCTGTA

25

A double stranded DNA loop of length 11.020 kilo-bases on chromosome 10 is bounded on the left by a T1 sequence whose identifier is 4295. This T1 control element has the DNA sequence

30

AAACGCAAGGATTGATAATGTAATAGGATCAATGAATATAAACATATAAA
ACCGAATGAGGAATAATCGTAATATTAGTATGTAGAAATATAGATTCCAT
TTGAGGATT CCTATATCCTCGAGGAGAACTCTAGTATATTCTG

5 This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 4308. This T2 control element has the DNA sequence

GGAAGCTGAAACGCAAGGATTGATAATGTAATAGGATCAATGAATATAA
ACATATAAAACGGAATGAGGAATAATCGTAATATTAGTATGTAGAAATAT
10 AGATTCCATTTGAGGATT CCTATATCCTCGAGGAGAACTCTAGTATATT
CTGTATACCTAATATTATAGCCTTATCAA

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

15 YJR027W YJR029W

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

20 A C1/C2 short loop on chromosome 1 whose identifier is 87 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YAR009C and has the DNA sequence

25 ATCTATTACATTATGGGTGGTATGTTGGAATAGAAATCAACTATCATCTAC
TAACTAGTATTTACATTACTAGTATATTATCATATACGGTGTAGAAGATG
ACGCAAATGATGAGAAATAGTCATCTAAATTAGTGGAGCTGAAACGCA
AGGATTGATAATGTAATAGGATCAATGAATATAAACATATAAACGGAAT
GAGGAATAATCGTAATATTAGTATGTAGAAATATAGATTCCATTTGAGG
30 ATTCCTATATCCTCGAGGAGAACTCTAGTATATTCTGTATACCTAATATT
ATAGCCTTATCAACAATGGAATCCCAACAATTATCTCAACACATTACCCAT
TTCTCA

5 A double stranded DNA loop of length 5.462 kilo-bases on chromosome 13 is bounded on the left by a T1 sequence whose identifier is 5916. This T1 control element has the DNA sequence

AAGCTGAAGTCAAGGATTGATAATGTAATAGGATAATGAAACATATAA
AACGGAATGAGGAATAATCGTAATATTAGTATGTAGAAATATAGATTCCA
10 TTTGAGGATTCCATATCCTCGAGGAGAACTTCTAGTATATTCTGTA

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 5923. This T2 control element has the DNA sequence

15 TAATAGGATAATGAAACATATAAACGGAATGAGGAATAATCGTAATATTAGTATGTAGAAATATAGATTCCATTTGAGGATTCCATATCCTCGAGGAGAACTTCTAGTATATTCTGTAACCTAACCTAATATTATAGCCTTATCAA

20 This long T1/T2 double stranded DNA loop modulates the expression of the following genes

YML045W

25 The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

30 A C1/C2 short loop on chromosome 1 whose identifier is 87 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YAR009C and has the DNA sequence

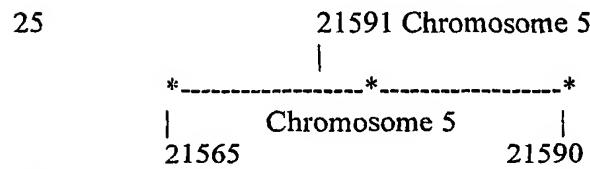
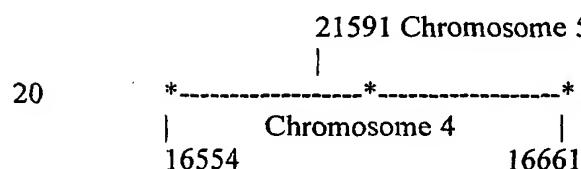
ATCTATTACATTATGGGTGGTATGTTGGAATAGAAATCAACTATCATCTAC
TAACTAGTATTACATTACTAGTATATTATCATATACGGTGTTAGAAGATG

ACGCAAATGATGAGAAATAGTCATCTAAATTAGTGGAGCTGAAACGCA
AGGATTGATAATGTAATAGGATCAATGAATATAAACATATAAAACGGAAT
GAGGAATAATCGTAATATTAGTAGTAAATATAGATTCCATTGAGG
ATTCCTATATCCTCGAGGAGAACTCTAGTATATTCTGTATACCTAATATT
5 ATAGCCTTATCAACAATGGAATCCAACAATTATCTAACATTACCCAT
TTCTCA

10 Example of a one-to-many connectron in multi-cell eukaryotes – C. elegans

In this example the existence of T1-T2 (16554-16661 and 21565-21590) long loops are controlled by one C1/C2 short loop (21591).

15



30

A double stranded DNA loop of length 50.159 kilo-bases on chromosome 4 is
35 bounded on the left by a T1 sequence whose identifier is 16554. This T1 control
element has the DNA sequence

TGCCTGAAAAAATTGGCTCCGAGTTAGGACACTGGGTGGTCAAAAAAT
TTTGTGACTATTGTCAAATGAAAGATCATAGTTGATAACATAAATTCCCAA
AGTTTCATAAAAATCGATACGCAGCGAACAAAGTTATCAATT

5 This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 16661. This T2 control element has the DNA sequence

CACTTGGGTGGTCAAAAAATTGTGATTATTGTCAAATGAAAGATCAT
GGTTGATAACATAAATTCCCAAAGTTCATAAAAATCGATACGCAGCGAA
10 CAAAGTTATGATTTGACCCGGAACCTATTGGAGACCTA

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

15 C23H5.7 C23H5.8a C23H5.3 C23H5.2 C23H5.9 C23H5.1

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

20 A C1/C2 short loop on chromosome 5 whose identifier is 21591 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene F25A2.1 and has the DNA sequence

25 TATTGTCAAATGAAAGATCATGGTTGATAACATAAATTCCACAATTTCAT
AAAAATCGATACGCAGCGAACAAAGTTATGATTTGACCCGGAACCTAT
TTGGAGACCTAATATT

The match between the T1 sequence and the C1/C2 sequence is

30 TTTCATAAAAATCGATACGCAGCGAACAAAGTTAT

The match between the T2 sequence and the C1/C2 sequence is

TATTGTCAAATGAAAGATCATGGTTGATAACATAAATTCCA

5

A double stranded DNA loop of length 18.142 kilo-bases on chromosome 5 is bounded on the left by a T1 sequence whose identifier is 21565. This T1 control element has the DNA sequence

10

CTCCGAGTTAGGACACTTGGGTGGACAAAAAATTTGTGACTATTGTCA
AATGAAAGATCATGGTTGATAA

15

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 21590. This T2 control element has the DNA sequence

TATTGTCAAATGAAAGATCATGGTTGATAACATAAATTCCCACAATTCAT
AAAAATCGATACGCAGCGAACAAAGTTATGATTTGACCCGGAACCTTAT
TTGGAGACCTAATA

20

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

T21H3.2 T21H3.1 F25A2.1

25

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

30

A C1/C2 short loop on chromosome 5 whose identifier is 21591 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene F25A2.1 and has the DNA sequence

TATTGTCAAATGAAAGATCATGGTTGATAACATAAATTCCCACAATTCAT
AAAAATCGATACGCAGCGAACAAAGTTATGATTTGACCCGGAACCTTAT
TTGGAGACCTAATATT

5 The match between the T1 sequence and the C1/C2 sequence is

TATTGTCAAATGAAAGATCATGGTTGATAA

The match between the T2 sequence and the C1/C2 sequence is

10

TATTGTCAAATGAAAGATCATGGTTGATAACATAAATTCCCACAATTCAT
AAAAATCGATACGCAGCGAACAAAGTTATGATTTGACCCGGAACCTTAT
TTGGAGACCTAATA

15

4. Connectrons occur between prokaryotes and their plasmids.

Connectron relationships exist between prokaryotes and their plasmids. These connectrons implement a control mechanism between the two genomes that makes it possible for them to form a symbiotic relationship. In the case of *D. radiodurans* the relationship is not symmetric. The *D. radiodurans* genome sends C1/C2 short loops to the MP1 plasmid.

Example of a prokaryote/plasmid connectron – *D. radiodurans*

10

In this example the existence of T1-T2 (2654-2694 and 2692-2749) long loops in chromosome 3 that is the plasmid MP1 are controlled by one C1/C2 short loop (16) in chromosome 1.

15

16 Chromosome 1
2768 Chromosome 3 (plasmid MP1)
2653 Chromosome 3 (plasmid MP1)

|

20

| Chromosome 3 (plasmid MP1) |
2654 2694
| 2693 |

25

16 Chromosome 1
2768 Chromosome 3 (plasmid MP1)
2693 Chromosome 3 (plasmid MP1)

|

30

| Chromosome 3 (plasmid MP1) |
2692 2749
| 2693 2695 |

35

A double stranded DNA loop of length 46.903 kilo-bases on chromosome 3 (plasmid MP1) is bounded on the left by a T1 sequence whose identifier is 2654. This T1 control element has the DNA sequence

5 CAGCGTTTCTCGCTGTCCTGGACGGCTGAACGCCCTGAATCTCTCCCG
GTATGCAGCCTGCTCGGAGAGTACGATTCGTCGTTGGCTGCACCGAAGTG
ACGATGGGCCATTCCGTGGGCGCGTTACACCAGGCGACTGTCAGTACA
GCAATCGAGAGTGGCTGATCAGCCCCTGTGCGTTCTGCCATCGACGC
CTCTTTACCGCAAAGCCGGTCAGCACACCGCACACCTCGGCTCGTCTG
GAATGGCTGTGCCGCGCGGACC

10 This double stranded DNA loop is bounded on the right by a T2 control element
whose identifier is 2694. This T2 control element has the DNA sequence

15 GCTGAACGCCCTGAATCTCTCCCGTATGCAGCCTGCTCGGAGAGTACGA
TTCGTGTTGGCTGCACCGAAGTGACGATGGGCCATTCCGTGGGCGCG
TTACACCAGGCGACTGTCAGTACAGCAATCGAGAGTGGCTGATCAGCCC
ACTGTGCGTTCTGCCATCGACGCCCTTTTACCGCAAAGCCGGTCAGCA
CACCGCACACCTCGGCTCGTCTGGAATGGCTGTGCCGCGCGAACCGAAC
GCGGAATCGAGCAATCCTGTTGT

20 This long T1/T2 double stranded DNA loop modulates the expression of the
following genes

25 DRB0020 DRB0021 DRB0022 DRB0023 DRB0024 DRB0025
DRB0027 DRB0030 DRB0032 DRB0033 DRB0034 DRB0035
DRB0037 DRB0038 DRB0039 DRB0041 DRB0042 DRB0043
DRB0044 DRB0045 DRB0047 DRB0051 DRB0052 DRB0054
DRB0055 DRB0057

30 This long T1/T2 double stranded DNA loop modulates the expression of the
following C1/C2 short loops

A C1/C2 short loop on chromosome 3 (plasmid MP1) whose identifier is 2693
controls the expression of the genes of one or more other T1/T2 long loops. This

C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene DRB0057 and has the DNA sequence

5 CTGATGGCCATCCTACAGTACGTTCTCAGCGCGGTCCCCTGCCTGCAGCAAGAC
GCAGCGGAATTCTGACCGTGCTCAGCGTTTCTCGCTGTTCTGG
AC

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

10 A C1/C2 short loop on chromosome 1 whose identifier is 16 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene DR0009 and has the DNA sequence

15 GCTGTGAAATCACCGCTCCAATGGGTCTGATGGCCATCCTACAGTACGTT
CTCAGCGCGGTCCCCTGCAGCAAGACGAGCGAATTCTGACCGTGCT
GCTCAGCGTTTCTCGCTGTTCTGGACGGCTGAACGCCCTGAATCTCTC
CCGGTATGCAGCCTGCTCGGAGAGTACGATTCTCG

20 The match between the T1 sequence and the C1/C2 sequence is

25 CAGCGTTTCTCGCTGTTCTGGACGGCTGAACGCCCTGAATCTCTCCCG
GTATGCAGCCTGCTCGGAGAGTACGATTCTCGCTGTTGGCTGCACCGAAGTG
ACGATGGGGCCATTCCGTGGGGCGCGTTACACCAAGGCGACTGTCAGTACA
GCAATCGAGAGTGGGCTGATCAGCCCACGTGCGTTCTGGCCATCGACGC
CTCTTTACCGCAAAGCCGGTCAGCACACCGCACACCTCGGCTCGTTCTG
GAATGGCTGTGCCCGCGCGGACC

30 The match between the T2 sequence and the C1/C2 sequence is

GCTGAACGCCCTGAATCTCTCCCGTATGCAGCCTGCTCGGAGAGTACGA
TTCGTCGGCTGCACCGAAGTGACGATGGGGCCATTCCGTGGGGCGCG
TTACACCAGGCGACTGTCAGTACAGCAATCGAGAGTGGGCTGATCAGCCC
ACTGTGCGTTCTGCCATCGACGCCTCTTCACCGCAAAGCCGGTCAGCA
5 CACCGCACACCTCGGCTCGTCTGGAATGGCTGTGCCGCGGACCGAAC
GCGGAATCGAGCAATCCTGTTGT

A C1/C2 short loop on chromosome 3 (plasmid MP1) whose identifier is 2768
controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is
10 expressed as a RNA single strand that is 3'UTR to the gene DRB0133 and has the
DNA sequence

GCTGTGAAATCACCGCTTCCAATGGGTCTGATGGCCATCCTACAGTACGTT
CTCAGCGCGGTCCCGCTGCGCAAGACGCAGCGGAATTCCCTGACCGTGCT
15 GCTCAGCGTTTCTCGCTGTTCCCTGGACGGCTGAACGCCCTGAATCTCTC
CCGGTATGCAGCCTGCTCGGAGAGTACGATTGCT

The match between the T1 sequence and the C1/C2 sequence is

20 CAGCGTTTCTCGCTGTTCCCTGGACGGCTGAACGCCCTGAATCTCTCCCG
GTATGCAGCCTGCTCGGAGAGTACGATTGCTGGCTGCACCGAAGTG
ACGATGGGGCCATTCCGTGGGCGCGTTACACCAGGCGACTGTCAGTACA
GCAATCGAGAGTGGGCTGATCAGCCCAGTGTGCGTTCTGCCATCGACGC
25 CTCTTTACCGCAAAGCCGGTCAGCACACCGCACACCTCGGCTCGTCTG
GAATGGCTGTGCCGCGCGGACC

The match between the T2 sequence and the C1/C2 sequence is

30 GCTGAACGCCCTGAATCTCTCCCGTATGCAGCCTGCTCGGAGAGTACGA
TTCGTCGGCTGCACCGAAGTGACGATGGGGCCATTCCGTGGGGCGCG
TTACACCAGGCGACTGTCAGTACAGCAATCGAGAGTGGGCTGATCAGCCC

ACTGTGCGTTCTGGCCATCGACGCCCTTTCACCGCAAAGCCGGTCAGCA
CACCGCACACCTCGGCTCGTCTGGAATGGCTGTGCCGCACGGACCGAAC
GCGGAATCGAGCAATCCTGTTGT

5 A C1/C2 short loop on chromosome 3 (plasmid MP1) whose identifier is 2653 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene DRB0017 and has the DNA sequence

10 CGGTCCCCGCTGCAGAAGACGCAGCGGAATTCCCTGACCGTGCTGCTCAGC
GTTTTCTCGCTGTTCTGGACGGCTGAACGCCCTGAATCTCTCCCGGTAT
GCAGCCTGCTCGGAGAGTACGATTGTCGTTGGCTGCACCGAAGTGACGA
TGGGGCCATTCCGTGGGGCGCGTTACACCAGGCGA

15 The match between the T1 sequence and the C1/C2 sequence is

CAGCGTTTCTCGCTGTTCTGGACGGCTGAACGCCCTGAATCTCTCCCG
GTATGCAGCCTGCTCGGAGAGTACGATTGTCGTTGGCTGCACCGAAGTG
ACGATGGGGCCATTCCGTGGGGCGCGTTACACCAGGCGACTGTCAGTACA
20 GCAATCGAGAGTGGCTGATCAGCCCAGTGCCTGACCGCATTCCGTGGCTGCACGC
CTCTTTACCGCAAAGCCGGTCAGCACACCGCACACCTCGGCTCGTTCTG
GAATGGCTGTGCCGCACGGACC

The match between the T2 sequence and the C1/C2 sequence is

25 GCTGAACGCCCTGAATCTCTCCCGGTATGCAGCCTGCTCGGAGAGTACGA
TTCGTCGTTGGCTGCACCGAAGTGACGATGGGGCCATTCCGTGGGGCGCG
TTACACCAGGCGACTGTCAGTACAGCAATCGAGAGTGGCTGATCAGCCC
ACTGTGCGTTCTGCCATCGACGCCCTTTCACCGCAAAGCCGGTCAGCA
30 CACCGCACACCTCGGCTCGTCTGGAATGGCTGTGCCGCACGGACCGAAC
GCGGAATCGAGCAATCCTGTTGT

5 A double stranded DNA loop of length 68.612 kilo-bases on chromosome 3 (plasmid MP1) is bounded on the left by a T1 sequence whose identifier is 2692. This T1 control element has the DNA sequence

10 CTGATGGCCATCCTACAGTACGTTCTCAGCGCGTCCCGCTGCGCAAGAC
GCAGCGGAATTTCCTGACCCTGCTGCTCAGCGTTTCTCGCTGTTCCCTGG
AC

15 This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 2749. This T2 control element has the DNA sequence

20 AGCGCGGTCCCGCTGCGCAAGACGCAGCGGAATTTCCTGACCGTGCTGCT
CAGCGTTTCTCGCTGTTCCCTGGACGGCTGAACGCCCTGAATCTCTCCCG
GT

25 This long T1/T2 double stranded DNA loop modulates the expression of the following genes

30 DRB0059 DRB0060 DRB0061 DRB0062 DRB0064 DRB0065
DRB0066 DRB0067 DRB0068 DRB0069 DRB0070 DRB0072
DRB0073 DRB0074 DRB0076 DRB0077 DRB0079 DRB0080
DRB0081 DRB0083 DRB0085 DRB0086 DRB0087 DRB0088
25 DRB0089 DRB0090 DRB0092 DRB0093 DRB0094 DRB0096
DRB0097 DRB0098 DRB0102 DRB0103 DRB0104 DRB0105
DRB0106 DRB0107 DRB0111 DRB0112

35 This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

A C1/C2 short loop on chromosome 3 (plasmid MP1) whose identifier is 2693 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene DRB0057 and has the DNA sequence

5

CTGATGGCCATCCTACAGTACGTTCTCAGCGCGTCCCCTGCAGCAAGAC
GCAGCGGAATTCTGACCGTGCTGCTCAGCGTTTCTCGCTGTTCTGG
AC

10

A C1/C2 short loop on chromosome 3 (plasmid MP1) whose identifier is 2695 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene DRB0057 and has the DNA sequence

15

GCTGAACGCCCTGAATCTCTCCGGTATGCAGCCTGCTCGGAGAGTACGA
TTCGTGTTGGCTGCACCGAAGTGACGATGGGGCCATTCCGTGGGGCGCG
TTACACCAGGCGACTGTCACTACAGCAATCGAGAGTGGGCTGATCAGCCC
ACTGTGCGTTCTGCCATCGACGCCCTTTTACCGCAAAGCCGGTCAGCA
CACCGCACACCTCGGCTCGTCTGGAATGGCTGTGCCGCGCGAACCGAAC
GCGGAATCGAGCAATCCTGTTGT

20

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

25

A C1/C2 short loop on chromosome 1 whose identifier is 16 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene DR0009 and has the DNA sequence

30

GCTGTGAAATACCGCTTCCAATGGGTCTGATGCCATCCTACAGTACGTT
CTCAGCGCGGTCCCGCTCGCAAGACGCAGCGGAATTCTGACCGTGCT
GCTCAGCGTTTCTCGCTGTTCCGGCTGAACGCCCTGAATCTCTC
CCGGTATGCAGCCTGCTCGGAGAGTACGATTGTT

The match between the T1 sequence and the C1/C2 sequence is

5 CTGATGGCCATCCTACAGTACGTTCTCAGCGCGTCCCGCTGCAGCAAGAC
GCAGCGGAATTTCCTGACCGTGCTGCTCAGCGTTTCTCGCTGTTCCCTGG
AC

The match between the T2 sequence and the C1/C2 sequence is

10 AGCGCGGTCCCCGCTGCAGCAAGACGCAGCGGAATTTCCTGACCGTGCTGCT
CAGCGTTTCTCGCTGTTCCCTGGACGGCTGAACGCCCTGAATCTCTCCCG
GT

15 A C1/C2 short loop on chromosome 3 (plasmid MP1) whose identifier is 2768
controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is
expressed as a RNA single strand that is 3'UTR to the gene DRB0133 and has the
DNA sequence

20 GCTGTGAAATACCGCTTCCAATGGGTCTGATGGCCATCCTACAGTACGTT
CTCAGCGCGTCCCGCTGCAGCAAGACGCAGCGGAATTTCCTGACCGTGCT
GCTCAGCGTTTCTCGCTGTTCCCTGGACGGCTGAACGCCCTGAATCTCTC
CCGGTATGCAGCCTGCTCGGAGAGTACGATTGT...CGGACCGAACGCGGA
ATCGAGCAATCCTGTTGTGCCCTCATTGATGTCCAGCACCGGCAGGCCTTG
ACGGTCGATGTCCGTCAAGACCCTGACCGGGCTGAGGCTCCAACTCGTCT
25 GGAACAG

The match between the T1 sequence and the C1/C2 sequence is

30 CTGATGGCCATCCTACAGTACGTTCTCAGCGCGTCCCGCTGCAGCAAGAC
GCAGCGGAATTTCCTGACCGTGCTGCTCAGCGTTTCTCGCTGTTCCCTGG
AC

The match between the T2 sequence and the C1/C2 sequence is

AGCGCGGTCCCCGCTGCGCAAGACGCAGCGGAATTCCCTGACCGTGCTGCT
CAGCGTTTTCTCGCTGTTCCCTGGACGGCTGAACGCCCTGAATCTCTCCCG
5 GT

A C1/C2 short loop on chromosome 3 (plasmid MP1) whose identifier is 2693 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene DRB0057 and has the
10 DNA sequence

CTGATGGCCATCCTACAGTACGTTCTCAGCGCGGTCCCCGCTGCGCAAGAC
GCAGCGGAATTCCCTGACCGTGCTGCTCAGCGTTTTCTCGCTGTTCCCTGG
AC
15

The match between the T1 sequence and the C1/C2 sequence is

CTGATGGCCATCCTACAGTACGTTCTCAGCGCGGTCCCCGCTGCGCAAGAC
GCAGCGGAATTCCCTGACCGTGCTGCTCAGCGTTTTCTCGCTGTTCCCTGG
20 AC

The match between the T2 sequence and the C1/C2 sequence is

AGCGCGGTCCCCGCTGCGCAAGACGCAGCGGAATTCCCTGACCGTGCTGCT
25 CAGCGTTTTCTCGCTGTTCCCTGGAC

A C1/C2 short loop on chromosome 3 (plasmid MP1) whose identifier is 2653 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene DRB0017 and has the
30 DNA sequence

CGGTCCCGCTGCGCAAGACGCAGCGGAATTCTGACCGTGCTGCTCAGC
GTTTTCTCGCTGTCCTGGACGGCTGAACGCCCTGAATCTCTCCCGTAT
GCAGCCTGCTCGGAGAGTACGATTGTCGTTGGCTGCACCGAAGTGACGA
TGGGGCCATTCCGTGGGGCGCGTTACACCAGGCGA

5

The match between the T1 sequence and the C1/C2 sequence is

C GG T C C C G C T G C G C A A G A C G C A G C G G A A T T C C T G A C C G T G C T G C T C A G C
G T T T T T C T C G C T G T C C T G G A C

10

The match between the T2 sequence and the C1/C2 sequence is

C GG T C C C G C T G C G C A A G A C G C A G C G G A A T T C C T G A C C G T G C T G C T C A G C
G T T T T T C T C G C T G T C C T G G A C G G C T G A A C G C C C T G A A T C T C T C C C G T

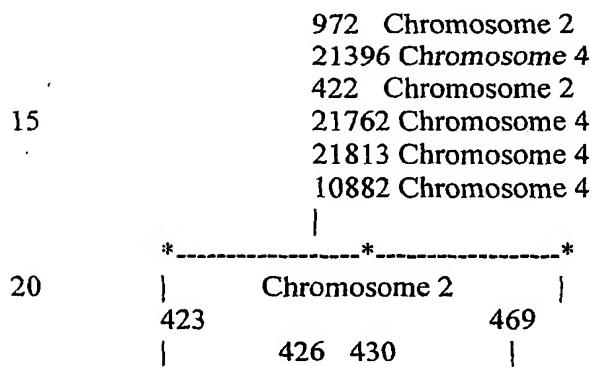
15

5. Connectrons occur in plants and higher animals

Connectron relationships exist in plant and higher animals.

5 Example of a plant connectron – A. thaliana

In this example the existence of the T1-T2 (423-469) long loop is controlled by six C1/C2 short loops (972, 21396, 422, 21762, 21813 and 10882). The T1-T2 long loop controls the expression of six genes on chromosome 2 in addition to two C1/C2 (426 and 430) short loops.



A double stranded DNA loop of length 42.285 kilo-bases on chromosome 2 is bounded on the left by a T1 sequence whose identifier is 423. This T1 control element has the DNA sequence

30 TATCTTTAAGGATTAAAAAGTCAAATACTAATTAAATTAAATTAAATTAA

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 469. This T2 control element has the DNA sequence

35

TACTAATTAAATTAAATTAAATTAAATTAAAAACGAAATACATTATTAATT
TTCAAAAATAATAACC

5 This long T1/T2 double stranded DNA loop modulates the expression of the
following genes

At2g02070 At2g02080 At2g02090 At2g02100 At2g02120 At2g02130

10 This long T1/T2 double stranded DNA loop modulates the expression of the
following C1/C2 short loops

15 A C1/C2 short loop on chromosome 2 whose identifier is 426 controls the expression
of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is
expressed as a RNA single strand that is 3'UTR to the gene At2g02060 and has the
DNA sequence

TTCCAAAAATAATAACCAATCAAAATCAACATATAAGATTGATATCTAA
ATTTT

20 A C1/C2 short loop on chromosome 2 whose identifier is 430 controls the expression
of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is
expressed as a RNA single strand that is 3'UTR to the gene At2g02060 and has the
DNA sequence

25 TTGCGGAAAAATAATATCATCATTATAAAAAATAATTAGAGTTTCGC
ATAT

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2
short loops.

30

A C1/C2 short loop on chromosome 2 whose identifier is 972 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene At2g04240 and has the DNA sequence

5 GTATGCCATTAGAAATAAAATTTAAAAGTAAATTAAATTCTCATCTCTTTAAA
AATTAAAAAGTCAAATACTAATTAAATTAAATTAAATTAAATTAAAAACG
AAATACATTATTAAATT

The match between the T1 sequence and the C1/C2 sequence is

10 ATTAAAAAGTCAAATACTAATTAAATTAAATTAAATTAAATTAAAAACGA
AATA

The match between the T2 sequence and the C1/C2 sequence is

15 TACTAATTAAATTAAATTAAATTAAATTAAATTAAATTAAATTAAATT
T

20 A C1/C2 short loop on chromosome 4 whose identifier is 21396 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene AT4g15300 and has the DNA sequence

25 TGCCATTAGAAATAAAATTTAAAGAGTAAATTAAATTCTCTTTAAGGA
TTAAAAAGTCAAATACTAATTAAATTAAATTAAATTAAATTAAAAACGAA
ATACATTATTAAATTCCAAAA

The match between the T1 sequence and the C1/C2 sequence is

30 TATCTCTTAAGGATTAAAAAGTCAAATACTAATTAAATTAAATTAAATT
ATTAAAAAACGAAATA

The match between the T2 sequence and the C1/C2 sequence is

TACTAATTAAATTAATTAAATTAAATTAAATTAAAAACGAAATACATTATTAATT
T

5

A C1/C2 short loop on chromosome 2 whose identifier is 422 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene At2g02060 and has the DNA sequence

10 TAACCTTAATTTGTAGTAATTATAGGTATGCCATTAGAAATAAAAT
TTTAAAGAGTAAATTAAATTATCTCTTAAGGATTAAAAGTCAAACTA
ATTTAATTAAATTAAATTAAATTAAAAACGAAATA

The match between the T1 sequence and the C1/C2 sequence is

15 TATCTCTTAAGGATTAAAAGTCAAACTAATTAAATTAAATTAAATTAA
ATTAAAAAACGAAATA

The match between the T2 sequence and the C1/C2 sequence is

20 TACTAATTAAATTAATTAAATTAAATTAAAAACGAAATA

A C1/C2 short loop on chromosome 4 whose identifier is 21762 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed 25 as a RNA single strand that is 3'UTR to the gene AT4g17510 and has the DNA sequence

TTTAAGGATTAAAAGTCAAACTAATTAAATTAAATTAAATTAAATTAA
AAACGAAATACATT

30

The match between the T1 sequence and the C1/C2 sequence is

TTTAAGGATTAAAAAGTCAAATACTAATTAAATTAAATTAAATTAAA
AAACGAAATA

The match between the T2 sequence and the C1/C2 sequence is

5

TACTAATTAAATTAAATTAAATTAAATTAAAAACGAAATACATT

A C1/C2 short loop on chromosome 4 whose identifier is 21813 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed
10 as a RNA single strand that is 3'UTR to the gene AT4g17680 and has the DNA sequence

TTTAAGGATTAAAAAGTCAAATACTAATTAAATTAAATTAAATTAAA
AAACGAAATACATT

15

The match between the T1 sequence and the C1/C2 sequence is

TTTAAGGATTAAAAAGTCAAATACTAATTAAATTAAATTAAATTAAA
AAACGAAATA

20

The match between the T2 sequence and the C1/C2 sequence is

TACTAATTAAATTAAATTAAATTAAATTAAAAACGAAATACATT

25

A C1/C2 short loop on chromosome 2 whose identifier is 10882 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene At2g26540 and has the DNA sequence

30

TATCTTTAAGGATTAAAAAGTCAAATACTAATTAAATTAAATTAAATTAA

The match between the T1 sequence and the C1/C2 sequence is

TATCTTTAAGGATTAAAAAGTCAAATACTAATTAAATTAAATTAAATTAA
ATTAA

5

The match between the T2 sequence and the C1/C2 sequence is

TACTAATTAAATTAAATTAAATTAAATTAA

10

Example of a animal connectron – D. megalomaster

A double stranded DNA loop of length 88.159 kilo-bases on chromosome 4 is
15 bounded on the left by a T1 sequence whose identifier is 3340. This T1 control
element has the DNA sequence

ACCTAAAAGAAGTACCGTTTTACTCCTAATTACCAATTCTAACCATCCA
TATCACTTTTGACGGACTCCGTGAAAATAATTGGCCAAATTCGCA
20 TTTTGTAAGGGTAACATCATAAAAATT

This double stranded DNA loop is bounded on the right by a T2 control element
whose identifier is 3372. This T2 control element has the DNA sequence

25 AAAAAAGTACCGCGTTTACTCCTAATTACCAATTCTAACCATCCATATCA
CTTTTGACGGACTCCGTGAAAATAATTGGCCAAATTCGCAATT
GTAAGGGGTAAACATCATCAAAATTGCGAAAAAA

30 This long T1/T2 double stranded DNA loop modulates the expression of the
following genes

[Some of the following gene names have not been determined.]

- - -
- CG11207 - CG2186 CG2157
- Ork1 - - -

5

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

10 A C1/C2 short loop on chromosome 4 whose identifier is 3362 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene XXX and has the DNA sequence

15 AAAAAAGTACCGCGTTTACTCCTAATTACCAATTCTAACCATCCATATCA
CTTTTGACGGACTCCGTTAAAATAATTTGACCAAATTTGCATTTTT
GTAATCAAAATTGCAAAAAATTGAAAAAAC

20 A C1/C2 short loop on chromosome 4 whose identifier is 3364 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene XXX and has the DNA sequence

25 CAAAATTGAATGCAAATCGATTGGAATCAAAAAACAAACTCAACGAG
GTATGACATTCCATATTGGGCCATTATTCCAA

30 A C1/C2 short loop on chromosome 4 whose identifier is 3366 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene XXX and has the DNA sequence

TTTTTCACAAAATTAGGAAAATGATTTGGTAAAAAAATGAATATT
AAGTTGGGTTT

5 A C1/C2 short loop on chromosome 4 whose identifier is 3369 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene XXX and has the DNA sequence

10 AAATCGATTGGGAATCAAAAAACAAACCTCAACGAGGTATGACATTCCAT
ATCTGGGCCATTATTCCAATCTTGATCAAAATAC

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

15 A C1/C2 short loop on chromosome 4 whose identifier is 3373 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene XXX and has the DNA sequence

20 AAAAAAGTACCGCGTTTACTCCTAATTACCAATTCTAACCATCCATATCA
CTTTTGACGGACTCCGTAAAATAATTGGCCAAATTCGCATTTT
GTAAGGGTAACATCATCAAAATTGCGAAAAA

The match between the T1 sequence and the C1/C2 sequence is

25 TTTTACTCCTAATTACCAATTCTAACCATCCATATCACTTTGACGGACTC
CGTAAAATAATTGGCCAAATTCGCATTTTGTAAAGGGTAACAT
CAT

30 The match between the T2 sequence and the C1/C2 sequence is

AAAAAAAGTACCGCGTTTACTCCTAATTACCAATTCTAACCATCCATATCA
CTTTTGACGGACTCCGTGAAAATAATTGGCAAATTCGCATTTTT
GTAAGGGGTAAACATCATCAAAATTGCGAAAAAA

5

Example of an animal connectron – H. sapiens

All of the human genome that has been fully sequenced by both the NIH-lead global sequencing project and the Celera Genomics, Inc. project. The gene descriptors for this chromosome do not yet exist. Without the positions and directions of the genes, it is not possible to select from among the possible connectrons to determine the real connectrons.

15 Human chromosome 22 has been processed and there 31,000 possible connectrons.

The gene descriptors for all the chromosomes of the human genome should become available within the year.

20

6. Permanent connectrons exist in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes.

5 C1/C2 short loops are normally expressed as the 3'UTR of some gene. A class of connectron relationships exist that permit one C1/C2 short loop to control the existence of one or more T1-T2 long loops without being subject to any expression controls other than those of the gene to which the C1/C2 is 3'UTR. These connectron relationships are described as "permanent". Permanent connectrons exist in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes.

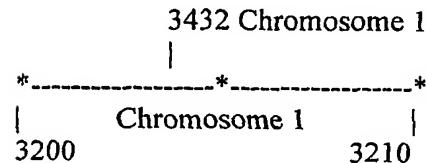
10

Example of a prokaryote permanent connectron – E. coli

15

In this example the existence of the T1-T2 (3200-3210) long loop is controlled by a C1/C2 short loop (3432). The expression of this C1/C2 short loop is controlled only by the gene *btuB*.

20



25

A double stranded DNA loop of length 93.339 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 3200. This T1 control element has the DNA sequence

30

AAGCGGCACTGCTTTAACAAATTATCAGACAATCTGTGTGGGACTCG
AAGATAACGGATTCTAACGTCGCAAGACGAAAAATGAATACCAAGTCTCA
AGAGTGAAACACGTAATTCAATTACGAAGTTAACATTCTTGAGCATCAAACCTT
TTAAATTGAAGAGTTGATCATGGCTCAGATTGAACGCTGGCGGCAGGCC
TAACACATGCAAGTCGAACGGTAACAGGAAACAGCAGCTTGCTGTTCGCTGA
CGAGTGGCGGACGGGTGAGTAATGTCTGGAAACTGCCTGATGGAGGGG

GATAACTACTGGAAACGGTAGCTAATACCGCATAACGTCGCAAGACCAAA
GAGGGGGACCTTCGGGCCTTGCATC

This double stranded DNA loop is bounded on the right by a T2 control element
5 whose identifier is 3310. This T2 control element has the DNA sequence

CAGACAATCTGTGTGGCACTCGAAGATAACGGATTCTAACGTCGCAAGA
CGAAAAATGAATACCAAGTCTCAAGAGTGAACACGTAATTACGAAG
TTAATTCTTGAGCGTCAAACCTTAAATTGAAGAGTTGATCATGGCTC
10 AGATTGAACGCTGGCGCAGGCCTAACACACATGCAAGTCGAACGGTAACA
GGAAGAAGCTGCTTCTTGCTGACGAGTGGCGGACGGGTGAGTAATGTC
TGGGAAACTGCCTGATGGAGGGGGATAACTACTGGAAACGGTAGCTAAT
ACCGCATAACGTCGCAAGACCAAAGAGGGGGACCTTCGGGCCTTGC
15 TCGGATGTGCCAGATGGGATTAGCTAGT

15

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

	rrsC	gltU	rriC	rrfC	aspT	trpT	yifA	yifE	yifB
20	ilvL	ilvG_1	ilvM	ilvE	ilvD	ilvA	ilvY	ilvC	ppiC
	b3776	rep	gppA	rhlB	trxA	rhoL	rho	rfe	wzzE
	wecB	rffH	wecD	wecE	wzxE	yifM_2	wecG	yifK	
	argX	hisR	leuT	proM	aslB	aslA	hemY	hemX	
	hemD	cyaA	cyaY	b3808	dapF	uvrD	b3814	corA	
25	yigF	yigG	rarD	yigI	pldA	recQ	yigJ	yigK	pldB
	yigL	yigM	metR	metE	ysgA	udp	yigN	ubiE	yigP
	b3836	yigU	yigW_1	rfaH	yigC	ubiB	fadA	fadB	
	pepQ	trkH	hemG						

30

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

A C1/C2 short loop on chromosome 1 whose identifier is 3432 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene *btuB* and has the DNA sequence

5 TGCAGCGGTCAAGAAAATTATTTAAATTCCCTCTTGTCAAGGCCGGAATAACT
CCCTATAATGCGCCACCACTGACACGGAACAAACGGCAAACACGCCGCCGG
GTCAGCGGGGTTCTCCTGAGAACTCCGGCAGAGAAAGCAAAAATAATG
CTTGAECTCTGTAGCGGAAGGCGTATTATGCACACC...TGCAACTCGACTC
CATGAAGTCGGAATCGCTAGTAATCGTGGATCAGAATGCCACGGTGAATA
10 CGTTCCCAGGCCTGTACACACCGCCCGTCACACCATGGGAGTGGGTGC
AAAAGAAGTAGGTAGCTAACCTCGGGAGGGCGCTTACCACTTTGTGAT
TCATGACTGGGTGAAGTCGTAACAAGGTAACCGTAGGGAACCTGCGGT
TGGATCACCTCCTTACCTAAAGAAGCGT

15 The match between the T1 sequence and the C1/C2 sequence is

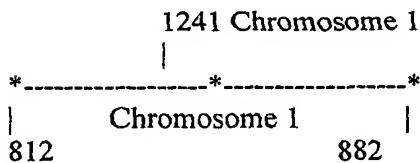
AAGCGGCACTGCTTTAACAAATTATCAGACAATCTGTGTGGGACTCG
AAGATAACGGATTCTAACGTGCAAGACGAAAAATGAATACCAAGTCTCA
AGAGTGAACACGTAATTACATTACGAAGTTAACCTTGTGAGC

20 The match between the T2 sequence and the C1/C2 sequence is

CAGACAATCTGTGTGGGACTCGAAGATAACGGATTCTAACGTGCAAGA
CGAAAAATGAATACCAAGTCTCAAGAGTGAACACCGTAATTACGAAG
25 TTAACCTTGTAGCGTCAAACCTTTAACATTGAAGAGTTGATCATGGCTC
AGATTGAACGCTGGCGGAGGCCTAACACATGCAAGTCGAACGGTAACA
GGAAGAAGCTTGCTTGTGACGAGTGGCGGACGGGTGAGTAATGTC
TGGGAAACTGCCTGATGGAGGGGATAACTACTGGAAACGGTAGCTAAT
ACCGCATAACGTGCAAGACCAAAGAGGGGGACCTCGGGCCTTGCCA
30 TCGGATGTGCCAGATGGGATTAGCTAGT

Example of an archaea permanent connectron – H. pylori

In this example the existence of the T1-T2 (812-882) long loop is controlled by a
 5 C1/C2 short loop (1241). The expression of this C1/C2 short loop is controlled only
 by the gene HP1535.



A double stranded DNA loop of length 96.385 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 812. This T1 control element has the DNA sequence

20 TTTTACTCATAGGGTTTTATAGTCCTAGCGGAACCAAAGCA

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 882. This T2 control element has the DNA sequence

25 TAGCGGAACCAAAGCATTCACTCCAAACACTAAAGATATTGG

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

30	HP0999	HP1000	HP1001	HP1002	HP1003	HP1005	HP1006
	HP1008	HP1009	HPtRNA-Pro	HP1010	HP1011	HP1013	HP1015
	HP1017	HP1018	HP1020	HP1021	HP1022	HP1023	HP1024
	HP1025	HP1027	HP1028	HP1030	HP1031	HP1033	HP1034
	HP1038	HP1039	HP1040	HP1041	HP1042	HP1043	HP1044

	HP1045	HP1046	HP1051	HP1052	HP1055	HP1056	HP1058
	HP1060	HP1065	HPtRNA-Ser	HP1066	HP1067	HP1069	HP1070
	HP1074	HP1075	HP1076	HP1077	HP1078	HP1079	HP1080
	HP1081	HP1083	HP1084	HP1085	HP1088	HP1091	HP1092
5	HP1093	HP1094	HP1095	HP1096			

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

10 A C1/C2 short loop on chromosome 1 whose identifier is 1241 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed, as a RNA single strand that is 3'UTR to the gene HP1535 and has the DNA sequence

15 TTTTACTCATAGGGTTTTATAGTCCTAGCGGAACCTAAAGCATTCCATCCC
AAACA

The match between the T1 sequence and the C1/C2 sequence is

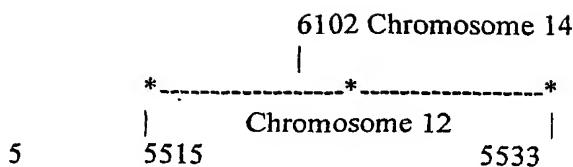
20 TTTTACTCATAGGGTTTTATAGTCCTAGCGGAACCTAAAGCA

The match between the T2 sequence and the C1/C2 sequence is

25 TAGCGGAACCTAAAGCATTCCATCCCAAACA

Example of a single-celled permanent connectron – S. cerevisiae

30 In this example the existence of the T1-T2 (5515-5533) long loop is controlled by a C1/C2 short loop (6102). The expression of this C1/C2 short loop is controlled only by the gene YNL339C.



10 A double stranded DNA loop of length 6.466 kilo-bases on chromosome 12 is bounded on the left by a T1 sequence whose identifier is 5515. This T1 control element has the DNA sequence

15 AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTGTAGTATAGTAT
ATTGTAAGAAATTCTAGGAAATATGCGTTGATGTAGTAGTAT
TTCACTGTTGATTTAGTGTGTTGCACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGTAGTAAGTAGCTTTGGTTG

20 This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 5533. This T2 control element has the DNA sequence

25 ATTATGTATTGTGTAGTATAGTATATTGTAAGAAATTCTAGGAA
ATATGCGTTGATGTAGTAGTATTCACTGTTGATTAGTGTGTTGC
ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAATC
TATAAAAGTAAACATAAAATAAGGTAGTAAGTAGCTTTGGTTGAACA
TCCGGGTAAGAGAGACAACAGGGCT

30 This long T1/T2 double stranded DNA loop modulates the expression of the following genes

YLR467W

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

A C1/C2 short loop on chromosome 14 whose identifier is 6102 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YNL339C and has the DNA sequence

5

AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTAGTATAGTAT
ATTGTAAGAAATTCTAGGAAATATCGCTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGACGGCAGTAGCGAGAGACAAGTG
10 GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTGGTTAACATCCGGTAAGAGAGACAACAGGGCT

10

The match between the T1 sequence and the C1/C2 sequence is

15

AGGAAATTGTTACGAAAGTCAGTGATTATGTATTGTAGTATAGTAT
ATTGTAAGAAATTCTAGGAAATATCGCTTGATGTAGTAGTAT
TTCACTGTTGATTAGTGTGACGGCAGTAGCGAGAGACAAGTG
GGAAAGAGTAGGATAAAAAGACAATCTATAAAAGTAAACATAAAATAA
AGGTAGTAAGTAGCTTGGTTG

20

The match between the T2 sequence and the C1/C2 sequence is

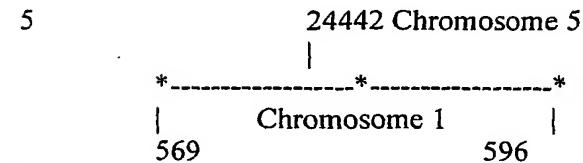
25

ATTATGTATTGTAGTATAGTATATTGTAAGAAATTCTAGGAA
ATATCGCTTGATGTAGTAGTATTCACTGTTGATTAGTGTGTTGC
ACGGCAGTAGCGAGAGACAAGTGGAAAGAGTAGGATAAAAAGACAATC
TATAAAAGTAAACATAAAATAAGGTAGTAAGTAGCTTGGTTAAC
TCCGGGTAAGAGACAACAGGGCT

30

Example of a multi-celled permanent connectron – *C. elegans*

In this example the existence of the T1-T2 (5515-5533) long loop is controlled by a C1/C2 short loop (6102). The expression of this C1/C2 short loop is controlled only by the gene YNL339C.



10

A double stranded DNA loop of length 30.606 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 569. This T1 control element has the DNA sequence

AAATCGAGCCCGTAAATCGACACAAGCGCTACAGTAGTC

15 This double stranded DNA loop is bounded on the right by a T2 control element
 20 whose identifier is 596. This T2 control element has the DNA sequence

AGTGCTACAGTAGTCATTAAAGAATTACTGTAGTTTCGCT

25 The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

30

A C1/C2 short loop on chromosome 5 whose identifier is 24442 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene F20D6.4 and has the DNA sequence

GAGCCCGTAAATCGACACAAGCGCTACAGTAGTCATTAAAGAATTACTG
 TAGTTTC

The match between the T1 sequence and the C1/C2 sequence is

GAGCCCGTAAATCGACACAAGCGCTACAGTAGTC

The match between the T2 sequence and the C1/C2 sequence is

5

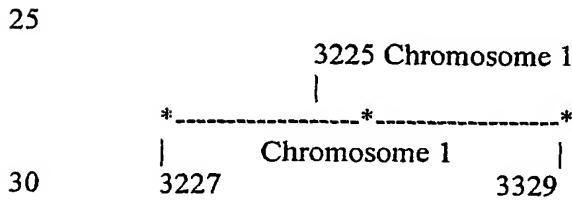
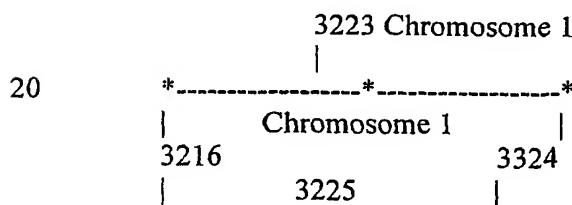
GCTACAGTAGTCATTAAAGAATTACTGTAGTTTC

7. Transient connectrons exist in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes.

5 A class of connectron relationships exist that permit one C1/C2 short loop to control the existence of one or more T1-T2 long loops such that this C1/C2 short loop is itself subject to expression control by another T1-T2 long loop which surrounds it. These connectron relationships are described as "transient". Transient connectrons exist in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes.

10 Example of a prokaryote transient connectron – E. coli

15 In this example the existence of the T1-T2 (3227-3329) long loop is controlled by the C1/C2 (3225) short loop. The expression of this C1/C2 short loop is controlled by the existence of the T1-T2 (3216-3224) long loop. The existence of this T1-T2 long loop is itself determined by the expression of the C1/C2 (3223) short loop. The C1/C2 (3225) short loop is the transient connectron.



35 A double stranded DNA loop of length 93.464 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 3216. This T1 control element has the DNA sequence

AGCGCAAGCGAAGCTCTGATCGAAGCCCCGGTAAACGGCGGCCGTAACT
 ATAACGGTCCTAACCGTAGCGAAATTCTTGTGGTAAGTCCGACCTGC
 ACGAATGGCGTAATGATGGCCAGGCTGTCTCCACCCGAGACTCAGTGAAA
 TTGAACTCGCTGTGAAGATGCAGTGTACCCGCCAGTGCATGGAGGCCACCT
 5 CGTGAACCTTACTATAGCTGACACTGAACATTGAGCCTGATGTGAGG
 ATAGGTGGGAGGCTTGAAGTGTGGACGCCAGTGCATGGAGGCCACCT
 TGAAATACCACCCTTAACGTTGATGTTCTAACGT

This double stranded DNA loop is bounded on the right by a T2 control element
 10 whose identifier is 3324. This T2 control element has the DNA sequence

CCCGGTAAACGGCGGCCGTAACTATAACGGTCCTAACCGTAGCGAAATTCC
 TTGTGGTAAGTCCGACCTGCACGAATGGCGTAATGATGCCAGGCTG
 TCTCCACCCGAGACTCAGTGAACATTGAACACTCGCTGTGAAGATGCAGTGTA
 15 CCCGCCAGACGGAAAGACCCGTGAACCTTACTATAGCTGACACT
 GAACATTGAGCCTGATGTGTAGGATAGGTGGAGGCTTGAAGTGTGGA
 CGCCAGTCTGCATGGAGCCGACCTGAAATACCAACCCTTAACGTTGATG
 TTCTAACGTTGACCCGTAAATCCGGGTTGCGGACAGT

20 This long T1/T2 double stranded DNA loop modulates the expression of the
 following genes

rrfC	aspT	trpT	yifA	yifE	yifB	ilvL	ilvG_1	ilvM
ilvE	ilvD	ilvA	ilvY	ilvC	ppiC	b3776	rep	gppA
25 rhlB	trxA	rhoL	rho	rfe	wzzE	wecB	rffH	wecD
wecE	wzxE	yifM_2	wecG	yifK	argX	hisR	leuT	
proM	aslB	aslA	hemY	hemX	hemD	cyaA	cyaY	
b3808	dapF	uvrD	b3814	corA	yigF	yigG	rarD	yigI
30 pldA	recQ	yigJ	yigK	pldB	yigL	yigM	metR	metE
ysgA	udp	yigN	ubiE	yigP	b3836	yigU	yigW_1	rfaH
yigC	ubiB	fadA	fadB	pepQ	trkH	hemG	rrsA	ileT
rrlA								

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

5 A C1/C2 short loop on chromosome 1 whose identifier is 3225 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene rrlC and has the DNA sequence

10 AACAGAATTGCCTGGCGGCCGTAGCGCGGTGGTCCCACCTGACCCCAT
GCCGAACTCAGAAGTGAAACGCCGTAGCGCCGATGGTAGTGTGGGTCTC
CCCATGCGAGAGTAGGAACTGCCAGGCATCAAATTA

15 The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

A C1/C2 short loop on chromosome 1 whose identifier is 3323 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene rrlA and has the DNA sequence

20 GCGAAGCTCTTATCGAAGCCCCGGTAAACGGCGGCCGTAACTATAACGG
TCCTAAGGTAGCGAAATTCTTGTGGTAAGTTCCGACCTGCACGAATG
GCGTAATGATGCCAGGCTGTCTCCACCCGAGACTCAGTGAAATTGAAC
CGCTGTGAAGATGCAGTGTACCCGGCAAGACGGA...AACAGAATTGC
25 CTGGCGGCAGTAGCGCGGTGGTCCCACCTGACCCATGCCGAACTCAGAA
GTGAAACGCCGTAGCGCCGATGGTAGTGTGGGTCTC

The match between the T1 sequence and the C1/C2 sequence is

30 GCGAAGCTCTTATCGAAGCCCCGGTAAACGGCGGCCGTAACTATAACGG
TCCTAAGGTAGCGAAATTCTTGTGGTAAGTTCCGACCTGCACGAATG
GCGTAATGATGCCAGGCTGTCTCCACCCGAGACTCAGTGAAATTGAAC

CGCTGTGAAGATGCAGTGTACCCGCGCAAGACGGAAAGACCCCGTGAA
CCTTTACTATAGCTTGACACTGAACATTGAGCCTGATGTGAGGATAGGT
GGGAGGCTTGAAGTGTGGACGCCAGTCGCATGGAGCCGACCTTGAAAT
ACCACCCCTTAATGTTGATGTTCAACGT

5

The match between the T2 sequence and the C1/C2 sequence is

CCCGTAAACGGCGGCCGTAACTATAACGGTCCTAAGGTAGCGAAATTCC
TTGTCGGGTAAGTCCGACCTGCACGAATGGCGTAATGATGCCAGGCTG
10 TCTCCACCCGAGACTCAGTGAATTGAACCTCGCTGTGAAGATGCAGTGT
CCCGCGGCAAGACGGAAAGACCCGTGAACCTTACTATAGCTTGACACT
GAACATTGAGCCTGATGTGAGGATAGGTGGGAGGCTTGAAGTGTGGA
GCCAGTCTGCATGGAGCCGACCTGAAATACCACCCCTTAATGTTGATG
TTCTAACGTTGACCGTAATCCGGTTGCGGACAGT

15

A double stranded DNA loop of length 93.749 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 3227. This T1 control element has the DNA sequence

AGCGCCGATGGTAGTGTGGGTCTCCCCATGCGAGAGTAGGAACTGCCA
GG

25

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 3329. This T2 control element has the DNA sequence

CATGCGAGAGTAGGAACTGCCAGGCATCAAATAACGAAAGGCTCAG
TCG

30

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

	aspT	trpT	yifA	yifE	yifB	ilvL	ilvG_1	ilvM	ilvE
	ilvD	ilvA	ilvY	ilvC	ppiC	b3776	rep	gppA	rhIB
	trxA	rhoL	rho	rfe	wzzE	wecB	rffH	wecD	wecE
5	wzxE	yifM_2	wecG	yifK	argX	hisR	leuT	proM	
	aslB	aslA	hemY	hemX	hemD	cyaA	cyaY	b3808	
	dapF	uvrD	b3814	corA	yigF	yigG	rarD	yigI	pldA
	recQ	yigJ	yigK	pldB	yigL	yigM	metR	metE	ysgA
	udp	yigN	ubiE	yigP	b3836	yigU	yigW_1	rfaH	yigC
10	ubiB	fadA	fadB	pepQ	trkH	hemG	rrsA	ileT	rriA
	rrfA								

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

15 A C1/C2 short loop on chromosome I whose identifier is 3225 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene rrlC and has the DNA sequence

20 AACACAGAATTGCCCTGGCGGCCGTAGCGCGGTGGTCCCACCTGACCCCAT
GCCGAACTCAGAAAGTGAAACGCCGTAGCGCCGATGGTAGTGTGGGGTCTC
CCCCATGCGAGAGTAGGAACTGCCAGGCATCAAATTA

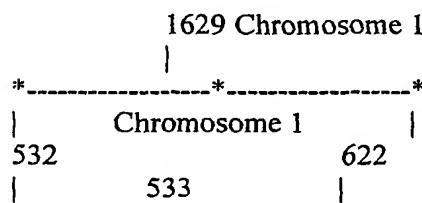
25 The match between the T1 sequence and the C1/C2 sequence is
AGCGCCGATGGTAGTGTGGGTCTCCCCATGCGAGAGTAGGAACTGCCA
GG

30 The match between the T2 sequence and the C1/C2 sequence is
CATGCGAGAGTAGGAACTGCCAGGCATCAAAT

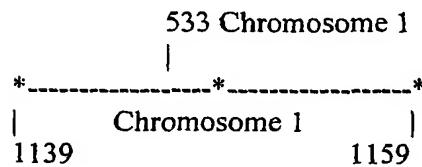
Example of an archea transient connectron – M. jannaschii

5 In this example the existence of the T1-T2 (1139-1159) long loop is controlled by the
C1/C2 (533) short loop. The expression of this C1/C2 short loop is controlled by the
existence of the T1-T2 (532-622) long loop. The existence of this T1-T2 long loop is
itself determined by the expression of the C1/C2 (1629) short loop. The C1/C2 (533)
short loop is the transient connectron.

10



15



20

A double stranded DNA loop of length 78.672 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 532. This T1 control element has the DNA sequence

30

ATATGTTGAAATTGAAAATAAGAGTATTAG

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 622. This T2 control element has the DNA sequence

35

TTGAAAATAAGAGCATTAGAAGTTATTAAATTAGTTCAAAGGATT

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

	MJ0486	MJ0487	MJ0488	MJ0489	MJ0490	MJ0492	MJ0493
5	MJ0494	MJ0495	MJ0496	MJ0497	MJ0499	MJ0500	MJ0501
	MJ0502	MJ0503	MJ0504	MJ0506	MJ0507	MJ0508	MJ0509
	MJ0510	MJ0511	MJ0512	MJ0513	MJ0514	MJ0514	MJ0517
	MJ0519	MJ0520	MJ0521	MJ0522	MJ0523	MJ0525	MJ0526
	MJ0526	MJ0529	MJ0530	MJ0531	MJ0532	MJ0534	MJ0535
10	MJ0536	MJ0538	MJ0539	MJ0540	MJ0541	MJ0542	MJ0543
	MJ0544	MJ0545	MJ0547	MJ0548	MJ0549	MJ0550	MJ0552
	MJ0553	MJ0554	MJ0555	MJ0556	MJ0557	MJ0558	MJ0559
	MJ0560	MJ0561	MJ0562	MJ0563	MJ0564	MJ0565	MJ0566
	MJ0568	MJ0569	MJ0570				

15

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

20 A C1/C2 short loop on chromosome 1 whose identifier is 533 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene MJ0485 and has the DNA sequence

25 ATTTTATTAATTCTAAGGGTAGCTGGTTGATTATTAGAATATTGA

GTTTATTGAATT

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

30 A C1/C2 short loop on chromosome 1 whose identifier is 1629 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene MJ1597 and has the DNA sequence

ATATGTTGAAATTGAAAATAAGAGTATTAGAAGTTATTAGTTCA
AAGGATTTTATTAAATTCTAACGGGTTGCTGGTTGATTATTAGAATAT
TTGAGTTATTGAATTATTCAGATTTAAAAATTA

5

The match between the T1 sequence and the C1/C2 sequence is

ATATGTTGAAATTGAAAATAAGAGTATTAG

10

The match between the T2 sequence and the C1/C2 sequence is

ATTTAGAAGTTATTAAATTAGTTCAAAGGATT

15

A double stranded DNA loop of length 14.509 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 1139. This T1 control element has the DNA sequence

20

ATTTATTAAATTAGTTCAAAGGATTATTAAATTCTAACGGGTTAGCTGG
TTTGATTGTTAAAATATTGAGTTA

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 1159. This T2 control element has the DNA sequence

25

ATTTAATTCTAACGGGTTAGCTGGTTGATTATTAGAATATTGAGTTAT
TGAATTATTCAGATTTAAAAATTA

30

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

MJ1096 MJ1097 tRNA-Arg-3 MJ1098 MJ1099 MJ1100 MJ1101
MJ1102 MJ1103 MJ1104 MJ1105 MJ1106 MJ1107 MJ1108

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2
5 short loops.

A C1/C2 short loop on chromosome 1 whose identifier is 533 controls the expression
of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA
single strand that is 3'UTR to the gene MJ0485 and has the DNA sequence
10

ATTTTATTAAATTCTAAGGGTAGCTGGTTGATTATTTAGAATATTGA
GTTTATTGAATT

The match between the T1 sequence and the C1/C2 sequence is

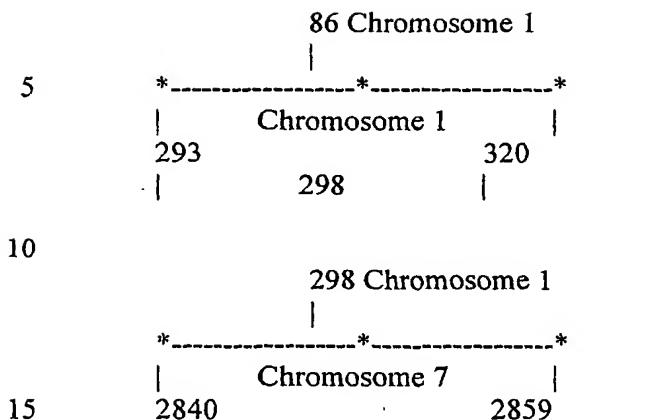
15 ATTTTATTAAATTCTAAGGGTAGCTGGTTGATT

The match between the T2 sequence and the C1/C2 sequence is

20 ATTTAATTCTAAGGGTAGCTGGTTGATTATTTAGAATATTGAGTTAT
TGAATT

25 Example of a single-celled transient connectron – S. cerevisiae

In this example the existence of the T1-T2 (2840-2859) long loop is controlled by the
C1/C2 (298) short loop. The expression of this C1/C2 short loop is controlled by the
existence of the T1-T2 (293-320) long loop. The existence of this T1-T2 long loop is
30 itself determined by the expression of the C1/C2 (86) short loop. The C1/C2 (298)
short loop is the transient connectron.



A double stranded DNA loop of length 38.470 kilo-bases on chromosome 2 is bounded on the left by a T1 sequence whose identifier is 293. This T1 control element has the DNA sequence

GAATTGTTGGAATAAAAATCCACTATCGTCTATCAACTAATAGTTATTA
TCAATATATTATCATATACGGTGTAAAGATGATGACATAAGTTATGAGAA
GCTGTCATCGAACGTTAGAGGAAGCTGAAGTGCAAGGATTGATAATGTAAT
AGGATAATGAAACATATAAAACGGAATGAGGAATAATCGTAATATTAGT
ATGTAGAAATATAGATTCCATTTCGAGGATTCCCTATATCCTTGAGGAGAAC
TTCTAGT

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 320. This T2 control element has the DNA sequence

AATATTAGTATGTAGAAATATAGATTCCATTGAGGATTCCCTATATCCTC
GAGGAGAACTCTAGTATATTCTGTA

35 This long T1/T2 double stranded DNA loop modulates the expression of the following genes

YBL005W-B TS(AGA)B YBL004W YBL003C YBL002W YBL001C
YBR001C YBR002C YBR003W YBR004C YBR005W YBR006W
YBR007C YBR008C YBR009C YBR010W YBR011C YBR012C

5

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

10 A C1/C2 short loop on chromosome 2 whose identifier is 298 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YBL005W-B and has the DNA sequence

15 ATCTATTACATTATGGGTGGTATGTTGGAATAAAATCCACTATCGTCTAT
CAACTAATAGTTATATTATCAATATATTATCATACGGTGTAAAGATGAT
GACATAAGTTATGAGAAGCTGTCATCGAAGTTAGAGGAAGCTGAAGTGCA
AGGATTGATAATGTAATAGGATAATGAAACATATAAACCGGAATGAGGA
ATAATCGTAATATTAGTATGTAGAAATATAGATTCCATTTGAGGATTCCCT
20 ATATCCTGAGGAGAACTCTAGTATATTCTGTATACCTAACATTATAGCC
TTTATCAACAATGGAATCCCAACAATTATCTAACATTC

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

25 A C1/C2 short loop on chromosome 1 whose identifier is 86 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YAR009C and has the DNA sequence

30 ATCTATTACATTATGGGTGGTATGTTGGAATAGAAATCAACTATCATCTAC
TAACTAGTATTACATTACTAGTATATTATCATACGGTGTAGAAGATG
ACGCAAATGATGAGAAATAGTCATCTAAATTAGTGGAAAGCTGAAACGCA
AGGATTGATAATGTAATAGGATCAATGAATATAAACATATAAACCGGAAT

GAGGAATAATCGTAATATTAGTATGTAGAAATATAGATTCCATTGAGG
ATTCCTATATCCTCGAGGAGAACTCTAGTATATTCTGTATACCTAATATT
ATAGCCTTATCAACAATGGAATCCAACAAATTATCTAACACATTCACCCAT
TTCTCAGAA

5

The match between the T1 sequence and the C1/C2 sequence is

AAACATATAAAACGGAATGAGGAATAATCGTAATATTAGTATGTAGAAAT
ATAGATTCCATTGAGGATTCCCTATATCCT

10

The match between the T2 sequence and the C1/C2 sequence is

AATATTAGTATGTAGAAATATAGATTCCATTGAGGATTCCCTATATCCTC
GAGGAGAACTCTAGTATATTCTGTA

15

20

A double stranded DNA loop of length 5.302 kilo-bases on chromosome 7 is bounded on the left by a T1 sequence whose identifier is 2840. This T1 control element has the DNA sequence

25

TCTGTTGGAATAAAATCCACTATCGTCTATCAACTAATAGTTATATTATC
AATATATTATCATATACGGTGTAAAGATGATGACATAAGTTATGAGAAGC
TGTCAATCGAAGTTAGAGGAAGCTGAAACGCAAGGATTGATAATGTAATAG
GATCAATGAATATAACATATAAAACGGAATGAGGAATAATCGTAATATT
AGTATGTAGAAATATAGATTCCATTGAGGATTCCCTATATCCTCGAGGAG
AACTTCTAGTATATTCTGTATACCTAAATTATAGCCTTATCAACAATGGA
ATCCCAACAA

30

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 2859. This T2 control element has the DNA sequence

CTATCAACTAATAGTTATATTCAATATATTATACGGTGTAAAGA
TGATGACATAAGTTATGAGAAGCTGTCATCGAAGTTAGAGGAAGCTGAAA
CGCAAGGATTGATAATGTAATAGGATCAATGAATATAAACATATAAAACG
GAATGAGGAATAATCGTAATATTAGTATGTAGAAATATAGATTCCATT
5 GAGGATT CCTATATCCTCGAGGAGAACTTCTAGTATATTCTGTATACCTAA
TATTATAGCCTTATCAACAATGGAATCCAAACAATTATCTAACACATTCA
ATATTCTCAT

10 The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

A C1/C2 short loop on chromosome 2 whose identifier is 298 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YBL005W-B and has the DNA sequence

15 ATCTATTACATTATGGGTGGTATGTTGGAATAAAAATCCACTATCGTCTAT
CAACTAATAGTTATATTATCAATATATTATCATACGGTGTAAAGATGAT
GACATAAGTTATGAGAAGCTGTCATCGAAGTTAGAGGAAGCTGAAGTGCA
AGGATTGATAATGTAATAGGATAATGAAACATATAAAACGGAATGAGGA
20 ATAATCGTAATATTAGTATGTAGAAATATAGATTCCATTGAGGATTCC
ATATCCTGAGGAGAACTTCTAGTATATTCTGTATACCTAACATTATAGCC
TTTATCAACAATGGAATCCAAACAATTATCTAACACATT

25 The match between the T1 sequence and the C1/C2 sequence is
TGTGGAATAAAAATCCACTATCGTCTATCAACTAATAGTTATATTATCAA
TATATTATCATACGGTGTAAAGATGATGACATAAGTTATGAGAAGCTG
TCATCGAAGTTAGAGGAAGCTGAA

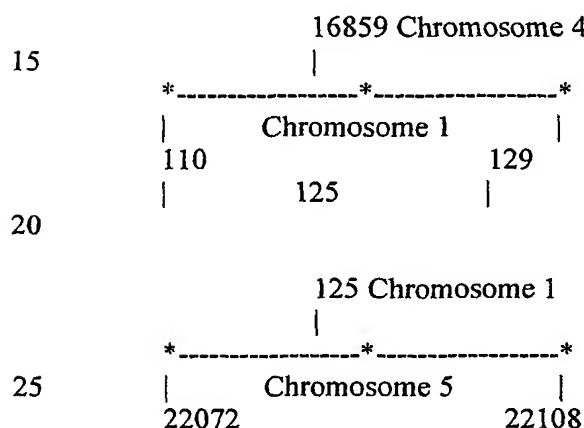
30 The match between the T2 sequence and the C1/C2 sequence is

CTATCAACTAATAGTTATATTATCAATATATTATCATATACGGTGTTAAGA
TGATGACATAAGTTATGAGAAGCTGTATCGAAGTTAGAGGAAGCTGAA

5

Example of a multi-celled transient connectron – C. elegans

In this example the existence of the T1-T2 (22072-22108) long loop is controlled by the C1/C2 (125) short loop. The expression of this C1/C2 short loop is controlled by the existence of the T1-T2 (110-129) long loop. The existence of this T1-T2 long loop is itself determined by the expression of the C1/C2 (16859) short loop. The C1/C2 (125) short loop is the transient connectron.



30 A double stranded DNA loop of length 18.855 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 110. This T1 control element has the DNA sequence

AGCTTAGGCTTAAGCTTAGGCTTAAGCTTAGGC

35

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 129. This T2 control element has the DNA sequence

TTCTCCCGCATTGGTAGATCTACGTAGATCAAACCGAAATGAGGCCT
TTCTGAATCCACGAGCTAGGCTTAAGCTTAGGCTTAAGCTTAGGCCTTTC
TCAGGCTTAGGCTTAGGCTTA

5

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

ZC123.3 ZC123.2

10

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

A C1/C2 short loop on chromosome 1 whose identifier is 125 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene ZC123.3 and has the DNA sequence

ACGCGCCGTAAATCTACCCCAGATATGGCCGAGCCAAAATGGCCTAGTTC
GGCAAACTCTTCATTCAATTATGAGGGAAGCCAGAA

20

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

25

A C1/C2 short loop on chromosome 4 whose identifier is 16859 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene F58E2.7 and has the DNA sequence

CTTAGGCTTAAGCTTAGGCTTAAGCTTAGGCTTAAGCTTAGGCTTAAGCTT
AGGCTTAAGCTTAGGCTTAAGCTTAGGCTTAAGCTTAGGCTTAAGCTTAG
GCTTAAGCTTAGGCTTAAGCTTAGGCTTAAGCTTAGGCTTAAGCTTAGGCT
TAAGCTTAGACTTA

The match between the T1 sequence and the C1/C2 sequence is

AGCTTAGGCTTAAGCTTAGGCTTAAGCTTAGGC

5

The match between the T2 sequence and the C1/C2 sequence is

TAGGCTTAAGCTTAGGCTTAAGCTTAGGC

10

A double stranded DNA loop of length 51.031 kilo-bases on chromosome 5 is bounded on the left by a T1 sequence whose identifier is 22072. This T1 control element has the DNA sequence

15

CGCAACGCGCCGTAAATCTACCCCAGATATGGCCGAGCCAAAATGACCTA
GTTCGGC

20

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 22108. This T2 control element has the DNA sequence

25

TGACAATCGCCTGCCGGACAACGCGTGGAAAAGTGTGCGTACTCCACAC
GGACAAATACATTAGTTTACAACATAAAATCGAACCGCGACGCGACACG
CAACGCGACGTAAATCTACCCCAGATATGGCCGAGCCAAAATGGCCTAGT
TCGGCAAACCTTTCTATTTC

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

30

F36H9.3 F36H9.4 F36H9.5 F36H9.2 F36H9.1 F36H9.6

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

5 A C1/C2 short loop on chromosome 1 whose identifier is 125 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene ZC123.3 and has the DNA sequence

ACGCGCCGTAAATCTACCCCAGATATGGCCGAGCCAAAATGGCCTAGTTC
GGCAAACTCTTCATTCAATTATGAGGGAAGCCAGAA

10

The match between the T1 sequence and the C1/C2 sequence is

ACGCGCCGTAAATCTACCCCAGATATGGCCGAGCCAAAATG

15

The match between the T2 sequence and the C1/C2 sequence is

CGTAAATCTACCCCAGATATGGCCGAGCCAAAATGGCCTAGTTGGCAA
CTCTT

20

8. Self-limiting connectrons occur in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes

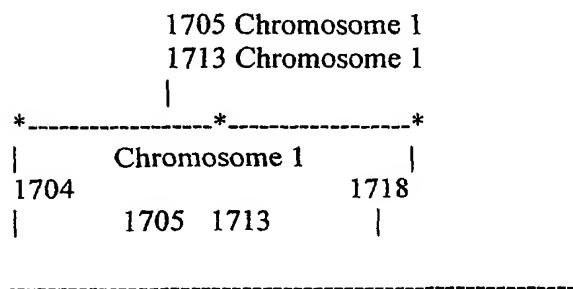
A class of connectron relationships exist that permit one C1/C2 short loop to control the existence of the T1-T2 long loop that surrounds it. These connectron relationships are described as "self-limiting". Self-limiting connectrons exist in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes.

Example of a prokaryotic self-limiting connectrons – E. coli

10

In this example the existence of the T1-T2 (1704-1718) long loop is controlled by two C1/C2 (1705 and 1713) short loops. The expression of these C1/C2 short loops is controlled by the existence of the T1-T2 (1704-1718) long loop. The existence of this T1-T2 long loop is itself determined by the expression of the two C1/C2 (1705 and 1713) short loops. The C1/C2 (1705 and 1713) short loops are the self-limiting connectrons.

20



25

30

A double stranded DNA loop of length 15.259 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 1704. This T1 control element has the DNA sequence

CGCCCCGTTCACACGATTCTCTGTAGTCAGTCGGTAGAACGGCGGACT
GTTAATCCGTATGTCACTGGT

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 1718. This T2 control element has the DNA sequence

5 TTCAGTCGGTAGAACGGCGGACTGTTAATCCGTATGTCACTGGTTCGAGTC
CAGTCAGAGGAGCCAAATT

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

10 asnT b1978 b1979 b1980 shiA amn b1983 asnW
yeeO asnU

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

15 A C1/C2 short loop on chromosome 1 whose identifier is 1705 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene and has the DNA sequence

20 CGCCCCGTTCACACGATTCCCTCTGTAGTTCAGTCGGTAGAACGGCGGACT
GTTAATCCGTATGTCACTGGTTCGAGTCAGAGGAGCCAAATT

25 A C1/C2 short loop on chromosome 1 whose identifier is 1713 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene asnW and has the DNA sequence

30 CACGATTCCCTCTGTAGTTCAGTCGGTAGAACGGCGGACTGTTAATCCGTAT
GTCACTGGTTCGAGTCAGAGGAGCCAAATT

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

5 A C1/C2 short loop on chromosome 1 whose identifier is 1705 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene and has the DNA sequence

CGCCCCGTTCACACGATTCCCTCTGTAGTCAGTCGGTAGAACGGCGGACT
GTTAATCCGTATGTCACTGGTTCGAGTCCAGTCAGAGGAGCCAAATT

10

The match between the T1 sequence and the C1/C2 sequence is

CGCCCCGTTCACACGATTCCCTCTGTAGTCAGTCGGTAGAACGGCGGACT
GTTAATCCGTATGTCACTGGT

15

The match between the T2 sequence and the C1/C2 sequence is

TTCAGTCGGTAGAACGGCGGACTGTTAATCCGTATGTCACTGGTTCGAGTC
CAGTCAGAGGAGCCAAATT

20

A C1/C2 short loop on chromosome 1 whose identifier is 1713 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene asnW and has the DNA sequence

25

CACGATTCCCTCTGTAGTCAGTCGGTAGAACGGCGGACTGTTAATCCGTAT
GTCACTGGTTCGAGTCCAGTCAGAGGAGCCAAATT

The match between the T1 sequence and the C1/C2 sequence is

30

CACGATTCCCTCTGTAGTCAGTCGGTAGAACGGCGGACTGTTAATCCGTAT
GTCACTGGT

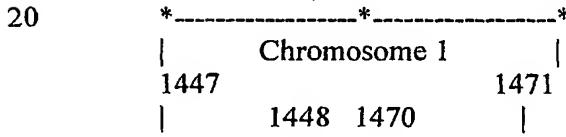
The match between the T2 sequence and the C1/C2 sequence is

TTCAGTCGGTAGAACGGCGGACTGTTAATCCGTATGTCACTGGTTCGAGTC
CAGTCAGAGGAGCCAAATT

5

Example of a archaea self-limiting connectrons – M. jannaschii

10 In this example the existence of the T1-T2 (1447-1471) long loop is controlled by two C1/C2 (1448 and 1470) short loops. The expression of these C1/C2 short loops is controlled by the existence of the T1-T2 (1447-1471) long loop. The existence of this T1-T2 long loop is itself determined by the expression of the two C1/C2 (1705 and 1713) short loops. The C1/C2 (1448 and 1470) short loops are the self-limiting
15 connectrons.



A double stranded DNA loop of length 22.675 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 1447. This T1 control element has the DNA sequence

30 TTATAGAACATTATGAAGCTTTACTCAACTAACAAACCGTATCGAATTAA
CCATTACTTGGAAATCTATTAAAACCTTTAATCTTATGATA

This double stranded DNA loop is bounded on the right by a T2 control element
35 whose identifier is 1471. This T2 control element has the DNA sequence

CAACTAACAAACCGTATCGAATTACCATTTGGAAATCTATTTAAAACC
TCTTTAATCTTGTGATAATAAATTCTAATCGATTCTGACTTAT

5 This long T1/T2 double stranded DNA loop modulates the expression of the following genes

MJ1402 MJ1403 MJ1404 MJ1405 MJ1406 MJ1407 MJ1408
MJ1409 MJ1410 MJ1411 MJ1412 MJ1413 MJ1414 MJ1415
10 MJ1416 MJ1417 MJ1418 MJ1419 MJ1420

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

15 A C1/C2 short loop on chromosome 1 whose identifier is 1448 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene MJ1401 and has the DNA sequence

20 TTATAGAACATTATGAAGCTTTACTCAACTAACAAACCGTATCGAATT
CCATTACTTGGAAATCTATTAAAACCTCTTAATCTTGTGATAATAAATT
CTAATCGATTCTGACTTAT

25 A C1/C2 short loop on chromosome 1 whose identifier is 1470 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene MJ1420 and has the DNA sequence

30 TTATAGAACATTATGAAGCTTTACTCAACTAACAAACCGTATCGAATT
CCATTACTTGGAAATCTATTAAAACCTCTTAATCTTGTGATAATAAATT
CTAATCGATTCTG

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

5 A C1/C2 short loop on chromosome 1 whose identifier is 1470 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene MJ1420 and has the DNA sequence

TTATAGAACATTATGAAGCTTTACTCAACTAACAAACCGTATCGAATT
CCATTACTTGGAAATCTATTAAAACCTCTTAATCTTGATAATAAATT
10 CTAATCGATTCTGTG

The match between the T1 sequence and the C1/C2 sequence is

15 TTATAGAACATTATGAAGCTTTACTCAACTAACAAACCGTATCGAATT
CCATTACTTGGAAATCTATTAAAACCTCTTAATCTT

The match between the T2 sequence and the C1/C2 sequence is

20 CAACTAACAAACCGTATCGAATTACCATTACTTGGAAATCTATTAAAACC
TCTTAATCTTGATAATAAATTCTAATCGATTCTGTG

A C1/C2 short loop on chromosome 1 whose identifier is 1448 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene MJ1401 and has the DNA sequence

25 TTATAGAACATTATGAAGCTTTACTCAACTAACAAACCGTATCGAATT
CCATTACTTGGAAATCTATTAAAACCTCTTAATCTTATGATAATAAATT
CTAATCGATTCTGTGACTTAT

30 The match between the T1 sequence and the C1/C2 sequence is

TTATAGAACATTATGAAGCTTTACTCAACTAACAAACCGTATCGAATTAA
CCATTACTTGGAAATCTATTAAAACCTCTTAATCTTATGATA

The match between the T2 sequence and the C1/C2 sequence is

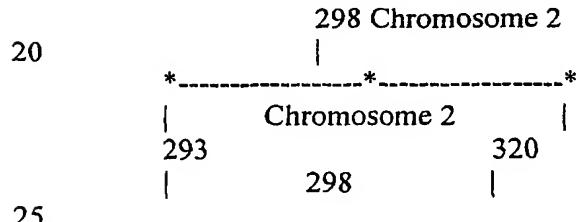
5

CAACTAACAAACCGTATCGAATTACCATTACTTGGAAATCTATTAAAACC
TCTTTAATCTT

10

Example of a single-celled self-limiting connectron – S. cerevisiae

In this example the existence of the T1-T2 (293-320) long loop is controlled by C1/C2 (298) short loop. The expression of this C1/C2 short loop is controlled by the existence of the T1-T2 (293-320) long loop. The existence of this T1-T2 long loop is itself determined by the expression of the C1/C2 (298) short loop. The C1/C2 (298) short loop is the self-limiting connectron.



A double stranded DNA loop of length 38.470 kilo-bases on chromosome 2 is bounded on the left by a T1 sequence whose identifier is 293. This T1 control element has the DNA sequence

30

GAATTGTTGGAATAAAAATCCACTATCGTCTATCAACTAATAGTTATATTA
TCAATATATTATCATATACGGTGTAAAGATGATGACATAAGTTATGAGAA
GCTGTCATCGAAGTTAGAGGAAGCTGAAGTGCAAGGATTGATAATGTAAT

AGGATAATGAAACATATAAAACGGAATGAGGAATAATCGTAATATTAGT
ATGTAGAAATATAGATTCCATTGAGGATTCCCTATACCTTGAGGAGAAC
TTCTAGT

5 This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 320. This T2 control element has the DNA sequence

AATATTAGTATGTAGAAATATAGATTCCATTGAGGATTCCCTATACCTC
GAGGAGAACTTCTAGTATATTCTGTA

10 15 This long T1/T2 double stranded DNA loop modulates the expression of the following genes

YBL005W-B TS(AGA)B YBL004W YBL003C YBL002W YBL001C
YBR001C YBR002C YBR003W YBR004C YBR005W YBR006W
YBR007C YBR008C YBR009C YBR010W YBR011C YBR012C

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

20 25 A C1/C2 short loop on chromosome 2 whose identifier is 298 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YBL005W-B and has the DNA sequence

ATCTATTACATTATGGGTGGTATGTTGGAATAAAAATCCACTATCGTCTAT
CAACTAATAGTTATATTATCAATATATTATCATACGGTGTAAAGATGAT
GACATAAGTTATGAGAAGCTGTCATCGAAGTTAGAGGAAGCTGAAGTGCA
AGGATTGATAATGTAATAGGATAATGAAACATATAAAACGGAATGAGGA
30 ATAATCGTAATATTAGTATGTAGAAATATAGATTCCATTGAGGATTCC
ATATCCTTGAGGAGAACTTCTAGTATATTCTGTATACCTAATATTATAGCC
TTTATCAACAATGGAATCCCAACAATTATCTAACATTC

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

5 A C1/C2 short loop on chromosome 2 whose identifier is 298 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YBL005W-B and has the DNA sequence

10 ATCTATTACATTATGGGTGGTATGTTGGAATAAAAATCCACTATCGTCTAT
CAACTAATAGTTATATTATCAATATATTATCATACGGTGTAAAGATGAT
GACATAAGTTATGAGAAGCTGTCATCGAAGTTAGAGGAAGCTGAAGTGCA
AGGATTGATAATGTAATAGGATAATGAAACATATAAACCGGAATGAGGA
ATAATCGTAATATTAGTATGTAGAAATATAGATTCCATTGAGGATTCCCT
ATATCCTTGAGGAGAACTCTAGTATATTCTGTATACCTAATATTATAGCC
15 TTTATCAACAATGGAATCCCAACAATTATCTCAACATTC

The match between the T1 sequence and the C1/C2 sequence is

20 TGTTGGAATAAAAATCCACTATCGTCTATCAACTAATAGTTATATTATCAA
TATATTATCATACGGTGTAAAGATGATGACATAAGTTATGAGAAGCTG
TCATCGAAGTTAGAGGAAGCTGAAGTGCAAGGATTGATAATGTAATAGGA
TAATGAAACATATAAACCGGAATGAGGAATAATCGTAATATTAGTATGTA
GAAATATAGATTCCATTGAGGATTCCCTATATCCTTGAGGAGAACTCTA
GT

25

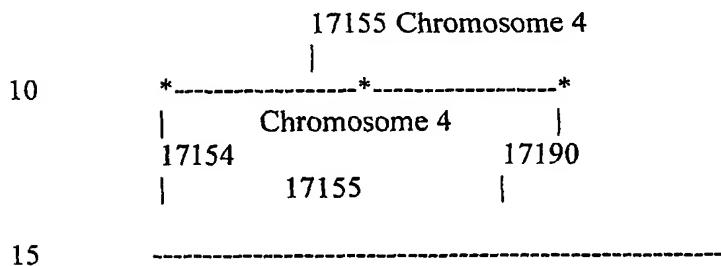
The match between the T2 sequence and the C1/C2 sequence is

AATATTAGTATGTAGAAATATAGATTCCATTGAGGATTCCCTATATCCT

30 -----

Example of a multi-celled self-limiting connectron – *C. elegans*

In this example the existence of the T1-T2 (293-320) long loop is controlled by C1/C2 (298) short loop. The expression of this C1/C2 short loop is controlled by the existence of the T1-T2 (293-320) long loop. The existence of this T1-T2 long loop is itself determined by the expression of the C1/C2 (298) short loop. The C1/C2 (298) short loop is the self-limiting connectron.



A double stranded DNA loop of length 89.919 kilo-bases on chromosome 4 is bounded on the left by a T1 sequence whose identifier is 17154. This T1 control element has the DNA sequence

20
AAATTCCGGCAAATCGGCAACTGGCAA

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 17190. This T2 control element has the DNA sequence

25
AATTTGCCGATTGCCGAATTGTCGACA

This long T1/T2 double stranded DNA loop modulates the expression of the following genes

30
R08C7.11 M01H9.2 M01H9.3 M01H9.4 M01H9.1 ZK180.1 ZK180.2
ZK180.3 ZK180.4 ZK180.5 ZK180.6 ZK185.3 ZK185.2

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

5 A C1/C2 short loop on chromosome 4 whose identifier is 17155 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene R08C7.1 and has the DNA sequence

10 AAATTCGGCAAATCGGAAACTGGCAATTGCCGATTGCCGAATTGT
CGACA

15 A C1/C2 short loop on chromosome 4 whose identifier is 17171 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene ZK180.2 and has the DNA sequence

TGGAAATTCAGAATTCAATTAAATCGGAAAATTGTACGCATCCTATG
AATTT

20 The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

25 A C1/C2 short loop on chromosome 4 whose identifier is 17155 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene R08C7.1 and has the DNA sequence

AAATTCGGCAAATCGGAAACTGGCAATTGCCGATTGCCGAATTGT
CGACA

30 The match between the T1 sequence and the C1/C2 sequence is

AAATTCGGCAAATCGGAAACTGGCAA

The match between the T2 sequence and the C1/C2 sequence is

AATTTGCCGATTTGCCGAATTTGTCGACA

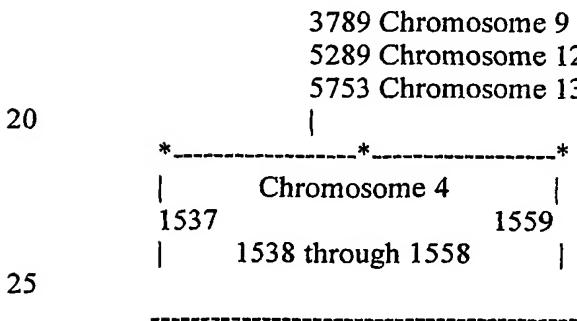
5

9. Geneless connectrons exist in single-celled and multi-celled eukaryotes

Normally T1-T2 long loops contain genes whose expression is regulated by the existence of the long loop. When a T1-T2 long loop does not contain any genes it is described as being "geneless". The existence of the T1-T2 long loop is itself controlled by one or more C1/C2 short loops that may be on the same or different chromosomes. The geneless T1-T2 long loops must contain one or more C1/C2 short loops.

10 Example of a single-celled geneless connectron – *S. cerevisiae*

In this example the existence of the T1-T2 (1537-1559) long loop is controlled by three C1/C2 (3789, 5289 and 5753) short loops. The expression of 21 C1/C2 (1538 through 1558) short loops are controlled by the existence of the T1-T2 (1537-1559) long loop.



A double stranded DNA loop of length 4.825 kilo-bases on chromosome 4 is bounded on the left by a T1 sequence whose identifier is 1537. This T1 control element has the DNA sequence

30
35 ATGAGATATATGTGGTAATTAGATAATTGTTGGATTCCATTGTTGATAA
AGGCTATAATATTAGGTATACAGAATATACTAGAAGTTCTCCTCGAGGAT
TTAGGAATCCATAAAAGGGAATCTGCAATTCTACACAATTCTATAAATAT
TATTATCATCGTTTATATGTTAATATTGATCCTATTACATTATCAAT

CCTTGCCTTCAGCTCCACTAATTAGATGACTATTCTCATCATTGCGT
CATCTCTAACACCGTATATGATAATATACTAGTAACGTAAACTAGTTA
GTAGATGATAGTTGATTTTATTCCAACATACCACCCATAATGTAATAGAT
CTAAT

5

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 1559. This T2 control element has the DNA sequence

10 ATGAGATATATGTGGGTAAATTAGATAATTGTTGGGATTCCATTGTTGATAA
AGGCTATAATATTAGGTATACAGAATATACTAGAAGTTCTCCTCGAGGAT
TTAGGAATCCATAAAAGGGAAATCTGCAATTCTACACAATTCTATAAATAT
TATTATCATCGTTTATATGTTAATATTGATCCTATTACATTATCAAT
CCTTGCCTTCAGCTCCACTAATTAGATGACTATTCTCATCATTGCGT
CATCTCTAACACCGTATATGATAATATACTAGTAACGTAAACTAGTTA
15 GTAGATGATAGTTGATTTTATTCCAACATACCACCCATAATGTAATAGAT
CTAAT

There are no genes controlled by this T1/T2 loop.

20 This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

A C1/C2 short loop on chromosome 4 whose identifier is 1538 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

25 ATGAGATATATGTGGGTAAATTAGATAATTGTTGGGATTCCATTGTTGATAA
AGGCTATAATATTAGGTATACAGAATATACTAGAAGTTCTCCTCGAGGAT
TTAGGAATCCATAAAAGGGAAATCTGCAATTCTACACAATTCTATAAATAT
TATTATCATCGTTTATATGTTAATATTGATCCTATTACATTATCAAT
CCTTGCCTTCAGCTCCACTAATTAGATGACTATTCTCATCATTGCGT
30 CATCTCTAACACCGTATATGATAATATACTAGTAACGTAAACTAGTTA

GTAGATGATAGTTGATTTTATTCCAACATACCAACCCATAATGTAATAGAT
CTAATGAATCCATTGTTGTTAATAGTTT

This T1-T2 loop also modulates the C1/C2 short loops numbered 1539 to 1557

5

A C1/C2 short loop on chromosome 4 whose identifier is 1558 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

10 AGCTTCTCATAACTTATGTCATCATCTAACACCGTATATGATAATATATT
GATAATATAACTTGGAAATAAAACTAACTATCATCTACTAACTAGTAT
TTACGTTACTAGTATATTATCATATACGGTGTAGAAGATGACGCAAATG
ATGAGAAAATAGTCATCTAAATTAGTGGAAAGCTGA...GTCTATCTGGCGAAT
15 ATAAATTTCACGCTACACACGTCATCGACATCTAAATATGACAGTCGCTG
AACTGTTCTTAGATATCCATGCTATTATGAAGAACAAACAGGGATCGAGA
AACAG

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

20

A C1/C2 short loop on chromosome 9 whose identifier is 3789 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YIL059C and has the DNA sequence

25

TTTATATGTTAATATTCAATTGATCCTATTACATTATCAATCCTTGCCTTCA
GCTTCCACTAATTAGATGACTATTCTCATCATTGCGTCATCTCTAAACA
CCGTATATGATAATATACTAGTAACGTAAATACTAGTTAGTAGATGATAG
TTGATTTTATTCCAACAGTAT

30

The match between the T1 sequence and the C1/C2 sequence is

TTTATATGTTAATATTCAATTGATCCTATTACATTATCAATCCTTGCCTTC
GCTTCCACTAATTAGATGACTATTCTCATCTTGCCTCATCTTCTAAC
CCGTATATGATAATATACTAGTAACGTAAACTAGTTAGTAGATGATAG
TTGATTTTATTCCAACA

5

The match between the T2 sequence and the C1/C2 sequence is

TTTATATGTTAATATTCAATTGATCCTATTACATTATCAATCCTTGCCTTC
GCTTCCACTAATTAGATGACTATTCTCATCTTGCCTCATCTTCTAAC
CCGTATATGATAATATACTAGTAACGTAAACTAGTTAGTAGATGATAG
TTGATTTTATTCCAACA

10

15

A C1/C2 short loop on chromosome 12 whose identifier is 5289 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YLR301W and has the DNA sequence

GGTGAATTTGAGATAATTGTTGGGATTCCATTTAATAAGGCAATAATA
TTAGGTATGTAGAATATACTAGAAGTTCTCCTCGAGGATTAGGAATCCAT
AAAAGGGAATCTGCAATTCTACACAATTCTATAAAATTATTATCATCGTT
TTATATGTTAATATTCAATTGATCCTATTACATTATCAATCCTTGCCTTCAG
CTTCCACTAATTAGATGACTATTCTCATCTTGCCTCATCTTCTAACAC
CGTATATGATAATATACTAGTAACGTAAACTAGTTAGTAGATGATAGT
TGATTTTATTCCAACAC

25

The match between the T1 sequence and the C1/C2 sequence is

AGAATATACTAGAAGTTCTCCTCGAGGATTAGGAATCCATAAAAGGGAA
TCTGCAATTCTACACAATTCTATAAAATTATTATCATCGTTATATGTTA
ATATTCAATTGATCCTATTACATTATCAATCCTTGCCTTCAGCTTCCACTAA
TTTAGATGACTATTCTCATCTTGCCTCATCTTCTAACACCCGTATATGAT

30

AATATACTAGTAACGTAAATACTAGTTAGTAGATGATAGTTGATTTTATT
CCAACA

The match between the T2 sequence and the C1/C2 sequence is

5 AGGATTAGGAATCCATAAAAGGAACTGCAATTCTACACAATTCTATA
AATATTATTATCATCGTTTATATGTTAATATTGATCCTATTACATTA
TCAATCCTGCCTTCAGCTTCACTAATTAGATGACTATTCTCATCATT
10 TGCGTCATCTCTAACACCGTATATGATAATATACTAGTAACGTAAACT
AGTTAGTAGATGATAGTTGATTTTATTCCAACA

A C1/C2 short loop on chromosome 13 whose identifier is 5753 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YMR044W and has the DNA sequence

15 TTGAGAAATGGGGAAATGTGAGATAATTGTTGGATTCCATTGATA
AAGGCTATAATATTAGGTATACAGAATATACTAGAAAGTTCTCCTCAAGGA
TATAGGAATCCTAAAATGGAATCTATATTCTACATACTAAATTACGAT
20 TATTCTCATTCCGTTTATATGTTCATTATCCTATTACATTATCAATCCT
TGCACITCAGCTTCTCTAACCTCGATGACAGCTCTCATAACTATGTCA
TCATCTAACACCGTATATGATAATATTGATAATATAACTATTAGTTGA
TAGACGATAGTGGATTTTATTCCAACAT

25 The match between the T1 sequence and the C1/C2 sequence is

AGATAATTGTTGGATTCCATTGTTGATAAAGGCTATAATATTAGGTATAC
AGAATATACTAGAAAGTTCTCCTC

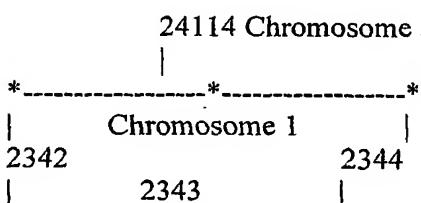
30 The match between the T2 sequence and the C1/C2 sequence is

TTGTTGGGATTCCATTGTTGATAAAGGCTATAATATTAGGTATACAGAATA
TACTAGAAGTTCTCCTCAAGGAT

5

Two examples of multi-celled geneless connectrons - C. elegans

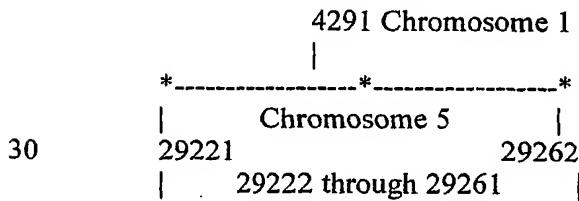
In the first example the existence of the T1-T2 (2342-2344) long loop is controlled by the C1/C2 (24114) short loop. The expression of one C1/C2 (2343) short loop is
10 controlled by the existence of the T1-T2 (2342-2344) long loop.



20

In the second example the existence of the T1-T2 (29221-29262) long loop is controlled by the C1/C2 (24114) short loop. The expression of one C1/C2 (2343) short loop is controlled by the existence of the T1-T2 (2342-2344) long loop.

25



35

A double stranded DNA loop of length 67.059 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 2342. This T1 control element has the DNA sequence

TGAAAACGTACAGTAATTCTTAAATGACTACTGTAGC

This double stranded DNA loop is bounded on the right by a T2 control element
5 whose identifier is 2344. This T2 control element has the DNA sequence

CTACTGTAGCGCTTGTGTCGATTACGGGCTCGATT

There are no genes controlled by this T1/T2 loop.

10

This long T1/T2 double stranded DNA loop modulates the expression of the
following C1/C2 short loops

15

A C1/C2 short loop on chromosome 1 whose identifier is 2343 controls the
expression of the genes of one or more other T1/T2 long loops. This C1/C2 short
loop has the DNA sequence

TCGACACAAGCGCTACAGTAGCTATTAAAGAATTACTGTAGTTTCGCTA
CGAGATATT

20

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2
short loops.

25

A C1/C2 short loop on chromosome 5 whose identifier is 24114 controls the
expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed
as a RNA single strand that is 3'UTR to the gene C13F10.5 and has the DNA
sequence

30

GCGAAAACGTACAGTAATTCTTAAATGACTACTGTAGCGCTTGTGTCGATT
TACGGGCTCGATTTCG

The match between the T1 sequence and the C1/C2 sequence is

GAAAAACTACAGTAATTCTTAAATGACTACTGTAGC

The match between the T2 sequence and the C1/C2 sequence is

5

CTACTGTAGCGCTTGTGTCGATTACGGGCTCGATT

10 A double stranded DNA loop of length 41.297 kilo-bases on chromosome 5 is bounded on the left by a T1 sequence whose identifier is 29221. This T1 control element has the DNA sequence

15 TTTAAATTCGGCCAAAAATTGACTGAAAATTGGATTTCTTCCAAAAA
ATTGACAGAAA

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 29262. This T2 control element has the DNA sequence

20 TGAAAATTGAATTCCGCCAAAAATTAAC

There are no genes controlled by this T1/T2 loop.

25 This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

A C1/C2 short loop on chromosome 5 whose identifier is 29222 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

30

AATTCCGCCAAAAATTGACTGAAAATTGGATTTCTTCCAAAAATTG
ACAGAAA

This T1-T2 loop also modulates the C1/C2 short loops numbered 29223 to 29260

5 A C1/C2 short loop on chromosome 5 whose identifier is 29261 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

AAAATTGACTGAAAATTGAATTCCAGCCAAAAATTGACTGAAAATTG
AATT

10

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

15 A C1/C2 short loop on chromosome 1 whose identifier is 4291 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene Y43F8C.5 and has the DNA sequence

20 AAAATTAAC TGAAAATTGAATTCCCGCCAAAAATTGACTGAAAATTG
AATTCCCGCCAAAAAAATTGACTGAAAATTGAATTCCCGCCAAAAA
TTGACTGAAAATTGAATTCCCGCCAAAAATTAAATTGAAAATTGAATT
CCCGCCAAAAATTAAATTGAAACTTGAATTTC...ATTCCCGCCAAAA
ATTAATTGAAACTTGAATTTC...ATTCCCGCCAAAAATTGACTGAAA
TTGAAATTCCCGCCAAAAATTAAATTGAAAATTGAATTTC...ATTCCC
25 GCCAAAAATGACTGA

The match between the T1 sequence and the C1/C2 sequence is

30 TTTAAATTCCCGCCAAAAATTGACTGAAAATTG

The match between the T2 sequence and the C1/C2 sequence is

AAAAAAATTGACTGAAAATTGAATTTCCCGCCAAAAATTGA

10. One connectron controls many geneless connectrons in single-celled and multi-celled eukaryotes

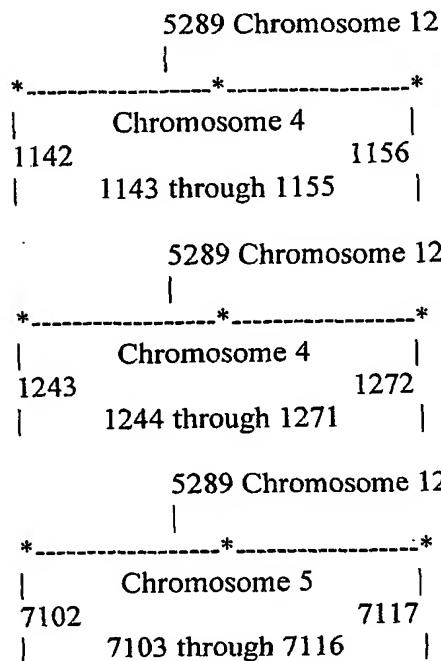
One C1/C2 short loop can control the existence of many geneless T1-T2 long loops.

5

Example of a single-celled geneless connectron – *S. cerevisiae*

In this example the existence of the three T1-T2 (1142-1156, 1242-1272 and 7102-7117) long loops is controlled by the C1/C2 (5289) short loop.

10



30

A double stranded DNA loop of length 5.337 kilo-bases on chromosome 4 is bounded on the left by a T1 sequence whose identifier is 1142. This T1 control element has the DNA sequence

ATTTGAGATAATTGTTGGGATTCCATTTTAATAAGGCAATAATATTAGG
TATGTAGATATACTAGAAGTTCTCCTCGAGGATTAGGAATCCATAAAAG

5 GGAATCTGCAATTCTACACAATTCTATAAATATTATTATCATCATTATA
TGTAAATATTGATTGATCCTATTACATTATCAATCCTTGCCTTCAGCTTCC
ACTAATTAGATGACTATTCTCATCTTGCCTCATCTTCTAACACCGTAT
ATGATAATATACTAGTAACGTAAACTAGTTAGTAGATGATAGTTGATT
TTATTCCAACA

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 1156. This T2 control element has the DNA sequence

10 TTTAATAAGGCAATAATATTAGGTATGTAGATATACTAGAAGTTCTCCTC
CAGGATTAGGAATCCATAAAAGGAACTGCAATTCTACACAATTCTAT
AAATATTATTATCATCATTATATGTTAATATTGATCCTATTACATT
ATCAATCCTTGCCTTCAGCTTCCACTAATTAGATGACTATTCTCATCAT
TTGCGTCATCTCTAACACCGTATATGATAATATACTAGTAACGTAAATAC
15 TAGTTAGTAGATGATAGTTGATTTTATTCCAACAAGAA

There are no genes controlled by this T1/T2 loop.

20 This long T1/T2 double stranded DNA loop modulates the expression of the
following C1/C2 short loops

A C1/C2 short loop on chromosome 4 whose identifier is 1143 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

25 ATTTGAGATAATTGTTGGGATTCCATTTAATAAGGCAATAATATTAGG
TATGTAGATATACTAGAAGTTCTCCTCGAGGATTAGGAATCCATAAAAG
GGAATCTGCAATTCTACACAATTCTATAAATATTATCATCATTATA
TGTAAATATTGATTGATCCTATTACATTATCAAT...CTCTAAGTCTCATTGCC
30 TTTGTGCCAAAAAAATCTGTTCTAAATTCTCTCATTGTAGACTTAATTA
TACTGATCGTTGATCTACTATCAGTAAGTAAGCCTTAATAATTGGTTCT
TGTAAAGTTCTGCACAAGGTGACTGAGGTTATTCAATAGCGG

This T1-T2 loop also modulates the C1/C2 short loops numbered 1144 to 1154

5 A C1/C2 short loop on chromosome 4 whose identifier is 1155 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

GAGGAGAACTTCTAGTATACATACATACTAATATTATTGCCTTATTAAAAA
ATGGAATCCCAACAATTA

10 The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

15 A C1/C2 short loop on chromosome 12 whose identifier is 5289 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YLR301W and has the DNA sequence

20 GGTGAATTTGAGATAATTGTTGGGATTCCATTITTAATAAGGCAATAATA
TTAGGTATGTAGAATATACTAGAAGTTCTCCTCGAGGATTAGGAATCCAT
AAAAGGGAATCTGCAATTCTACACAATTCTATAAAATATTATTATCATCGTT
TTATATGTTAATATTCAATTGATCCTATTACATTATCAATCCTTGCCTTCAG
CTTCCACTAATTAGATGACTATTCTCATCATTGCGTCATCTTCTAACAC
CGTATATGATAATATACTAGTACGTAAATACTAGTTAGTAGATGATAGTT
25 GATTITATTCCAACAC

The match between the T1 sequence and the C1/C2 sequence is

30 ATTTGAGATAATTGTTGGGATTCCATTITTAATAAGGCAATAATATTAGG
TATGTAGA

The match between the T2 sequence and the C1/C2 sequence is

TTTAATAAGGCAATAATATTAGGTATGTAGA

5

A double stranded DNA loop of length 5.251 kilo-bases on chromosome 4 is bounded on the left by a T1 sequence whose identifier is 1243. This T1 control element has the DNA sequence

10 CGTGTTCATGTTGTCGTTGTTATTGAGATATATGTGGTAATT
AGATAATTGTTGGGATTCCATTGTTGATAAAGGCTATAATATTAGGTATAC
AGAATATACTAGAACGTTCTCCTCGAGGATTAGGAATCCATAAAAGGGAA
TCTGCAATTCTACACAATTCTATAAAATTATTATCATGTTTATATGTTA
ATATTCAATTGATCCTATTACATTATCAATCCTGCCTTCAGCTTCCACTAA
15 TTTAGATGACTATTCTCATCATTGCGTCATCTCTAACACCGTATATGAT
AATATACTAGTAACGTAAACTAGTTAGTAGATGATAGTTGATTITATT
CCAACA

This double stranded DNA loop is bounded on the right by a T2 control element
20 whose identifier is 1272. This T2 control element has the DNA sequence

25 TGAGATATATGTGGTAATTAGATAATTGTTGGGATTCCATTGTTGATAAAA
GGCTATAATATTAGGTATACAGAATATACTAGAACGTTCTCCTCGAGGATT
AGGAATCCATAAAAGGAATCTGCAATTCTACACAATTCTATAAAATATTA
TTATCATCGTTTATATGTTAATATTCAATTGATC..TATACTAGTAACGTAA
ATACTAGTTAGTAGATGATAGTTGATTTTATTCCAACAGTTATAAGGTTG
TTTCATATGTGTTTATGAA

There are no genes controlled by this T1/T2 loop.

30

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

A C1/C2 short loop on chromosome 4 whose identifier is 1244 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

5

TTTATCTCATGTTGTCGTTGTTATTGAGATATATGTGGGTAAATTAGATA
ATTGTTGGGATTCCATTGTTGATAAAGGCTATAATATTAGGTATACAGAAT
ATACTAGAACGTTCTCCTCGAGGATTAGGAATCCATAAAAGGGAATCTGC
AATTCTACACAATTCTATAAAATTATTATTCAT...GTCTCGATGTAGTATAC
10 GTATAAATTATTACCTGATACTTCATCTCAAGTCTCATTCATTGCCTTGCCAA
AAAAATCTGTTCTAAATTCTCTTCATTGTAGACTTAATTACTGATCG
TTGATCTACTATCAGTAAGT

10

This T1-T2 loop also modulates the C1/C2 short loops numbered 1245 to 1270

15

A C1/C2 short loop on chromosome 4 whose identifier is 1271 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

20

TGTTGTATCTAAAATGAGATATGTCAGTATGACAATACGTCATCCTAAAC
GTTCATAAAACACATATGAAACAACCTTATAACTGTTGGAATAAAATCA
ACTATCATCTACTAACTAGTATTACGTTACTAGTATATTATCATATACGG
TGTAGAACGATGACGCAAATGATGAGAAATAGTC..CAACAATGGAATCC
25 CAACAATTATCTAATTACCCACATATCTCATGGTAGCGCCTGTGCTTCG
GTTACTTCTAAGGAAGTCCACACAAATCAAGATCCGTTAGACGTTTCAGC
TTCCAAAAA

25

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

30

A C1/C2 short loop on chromosome 12 whose identifier is 5289 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed

as a RNA single strand that is 3'UTR to the gene YLR301W and has the DNA sequence

5 GGTGAATTTGAGATAATTGTTGGGATTCCATTTTAATAAGGCAATAATA
TTAGGTATGTAGAATATACTAGAAGTTCTCCTCGAGGATTAGGAATCCAT
AAAAGGGAATCTGCAATTCTACACAATTCTATAAAATATTATTATCATCGTT
TTATATGTTAATATTCAATTGATCCTATTACATTATCAATCCTTGCCTTCAG
CTTCCACTAATTAGATGACTATTCTCATCTTGCCTCATCTAACAC
CGTATATGATAATATACTAGTAACGTAAACTAGTTAGTAGATGATAGT
10 TGATTTTATTCCAACAC

The match between the T1 sequence and the C1/C2 sequence is

15 AGAATATACTAGAAGTTCTCCTCGAGGATTAGGAATCCATAAAAGGGAA
TCTGCAATTCTACACAATTCTATAAAATATTATTATCATCGTTTATATGTTA
ATATTCAATTGATCCTATTACATTATCAATCCTTGCCTTCAGCTTCCACTAA
TTTAGATGACTATTCTCATCTTGCCTCATCTTCTAACACCGTATATGAT
AATATACTAGTAACGTAAACTAGTTAGTAGATGATAGTTGATTTTATT
CCAACA

20 The match between the T2 sequence and the C1/C2 sequence is

25 AGAATATACTAGAAGTTCTCCTCGAGGATTAGGAATCCATAAAAGGGAA
TCTGCAATTCTACACAATTCTATAAAATATTATTATCATCGTTTATATGTTA
ATATTCAATTGATCCTATTACATTATCAATCCTTGCCTTCAGCTTCCACTAA
TTTAGATGACTATTCTCATCTTGCCTCATCTTCTAACACCGTATATGAT
AATATACTAGTAACGTAAACTAGTTAGTAGATGATAGTTGATTTTATT
CCAACA

30 -----

A double stranded DNA loop of length 5.296 kilo-bases on chromosome 15 is bounded on the left by a T1 sequence whose identifier is 7102. This T1 control element has the DNA sequence

5 CATGATTAATATGACCAATCGCGTGTGTTTGAAAAGTGGGTGAATTT
GAGATAATTGTTGGGATTCCATTTAATAAGGCAATAATATTAGGTATGT
AGAATGTACTAGAACAGTTCTCCTCAAGGATTAGGAATCCATGAAAGGGAA
TCTGCAATTCTACACAATTCTATAAAATATTATTATCATCATTATATGTTA
10 ATATTCAATTGATCCTATTACATTATCAATCCTTGCCTTCAGCTTCCACTAA
TTTAGATGACTATTCTCATCATTGCGTCATCTCTAACACCGTATATGAT
AATATACTAGTAACGTAAATACTAGTTAGTAGATGATAGTTGATTTTATT
CCAACA

15 This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 7117. This T2 control element has the DNA sequence

TGAAAAGTGGGTGAATTTGAGATAATTGTTGGGATTCCATTTAATAAG
GCAATAATATTAGGTATGTAGAACAGTTCTCCTCAAGGATT
20 AGGAATCCATGAAAGGAAATCTGCAATTCTACACAATTCTATAAAATATTA
TTATCATCATTATGTTAATATTCAATTGATCCTATTACATTATCAATCC
TTGCGTTTCAGCTTCCACTAATTAGATGACTATTCTCATCATTGCGTCA
TCTCTAACACCGTATATGATAATATACTAGTAACGTAAATACTAGTTAGT
AGATGATAGTTGATTTATTCAAACAGTTATACCTCTTATTAGT
25 ATAAGAA

There are no genes controlled by this T1/T2 loop.

30 This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

A C1/C2 short loop on chromosome 15 whose identifier is 7103 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

5 AAGAACATTGCTGATGTGATGACAAAACCTCTCCGATAAAAACATTAA
ACTATTAACAAACAAATGGATTCAATTAGATCTATTACATTATGGGTGGTAT
GTTGGAATAAAAATCAACTATCATCTACTAACTAGTATTACGTTACTAGT
ATATTATCATATACGGTGTAGAAGATGACGCAAATGATGAGAAATAGTC
10 ATCTAAATTAGTGGAAAGCTGAAACGCAAGGATTGATAATGTAATAGGATC
AATGAATATTAACATATAAAATGATGATAATAATTTATAGAATTGTGT
AGAATTGCAGATTCCCTTCATGGATTCTAAATCCTGAGGAGAACTTCT
AGTA

This T1-T2 loop also modulates the C1/C2 short loops numbered 7104 to 7115

15 A C1/C2 short loop on chromosome 15 whose identifier is 7116 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

20 CCATTCTGTGGAGGTGGTACTGAAGCAGGTTGAGGAGAGACATGATGATG
GTTCTCTGGAACAGCT

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

25 A C1/C2 short loop on chromosome 12 whose identifier is 5289 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene YLR301W and has the DNA sequence

30 GGTGAATTTGAGATAATTGTTGGGATTCCATTTAATAAGGCAATAATA
TTAGGTATGTAGAATATACTAGAAGTTCTCGAGGATTAGGAATCCAT

5 AAAAGGGAATCTGCAATTCTACACAATTCTATAAATATTATTATCATCGTT
 TTATATGTTAATATTGATCCTATTACATTATCAATCCTGCGTTTCAG
 CTTCCACTAATTTAGATGACTATTCTCATCTTGCATCTTCTAACAC
 CGTATATGATAATATACTAGTAACGTAAACTAGTTAGTAGATGATAGT
 TGATTTTATTCCAACAC

The match between the T1 sequence and the C1/C2 sequence is

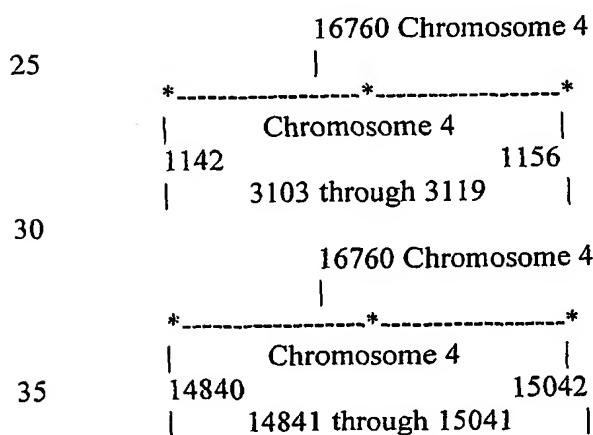
10 GGTGAATTTGAGATAATTGTTGGGATTCCATTTTAATAAGGCAATAATA
 TTAGGTATGTAGAAT

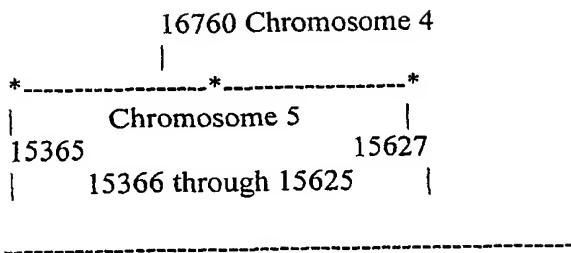
The match between the T2 sequence and the C1/C2 sequence is

15 GGTGAATTTGAGATAATTGTTGGGATTCCATTTTAATAAGGCAATAATA
 TTAGGTATGTAGAAT

 Example of a multi-celled geneless connectron - C. elegans

20 In this example the existence of the three T1-T2 (1142-1156, 14840-15042 and
 15365-15627) long loops is controlled by the C1/C2 (16760) short loop.





10 A double stranded DNA loop of length 15.894 kilo-bases on chromosome 1 is bounded on the left by a T1 sequence whose identifier is 3101. This T1 control element has the DNA sequence

15 CAAATCGGCAAATTGCCGGAATTGAACATTCC

This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 3120. This T2 control element has the DNA sequence

20 AAACGATTTCGGCAAATCGGCAAATTGCCGGAATTGTAATTCCGGC
AAAT

There are no genes controlled by this T1/T2 loop.

25 This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

30 A C1/C2 short loop on chromosome 1 whose identifier is 3103 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

TTAAAATTCCGGCAAATCGGCAAATTGGCAGAAATGAAACTCACGGCAA
ATCGG

35 This T1-T2 loop also modulates the C1/C2 short loops numbered 3104 to 3118

A C1/C2 short loop on chromosome 1 whose identifier is 3119 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

5

CCCGCATTTTGTAGATCAAACCGTAATGGGACGGCCTGGCAACACGTG
ATTTCCAAAT

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2

10 short loops.

A C1/C2 short loop on chromosome 4 whose identifier is 16760 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene T23E1.2 and has the DNA sequence

15

GGCAAATTGCCGAAATTGAACATTCCGGCAAATCGGCAAATTGCCGGAA
TTGAACATTCCGGCAAATCGGCAAATTGCCGGATTGAACATTCCGGC
AAATCGGCAAATTGCCGGATTGA

20

The match between the T1 sequence and the C1/C2 sequence is

CAAATCGGCAAATTGCCGGATTGAACATTCC

The match between the T2 sequence and the C1/C2 sequence is

25

TTTCCGGCAAATCGGCAAATTGCCGGATTG

30

A double stranded DNA loop of length 86.977 kilo-bases on chromosome 3 is bounded on the left by a T1 sequence whose identifier is 14840. This T1 control element has the DNA sequence

AAAAATTCGGCAAGTCGGAATTTCCGAAAATGAAAATTCCGGCAA
ATCGGCAAATTGCCCGAATTGAAAATTCCCTGGCAAATCAGCAAATTGCG
GCAAATCGGCAATTGCCGAAAATGAAAATTCCGGCAAAT

5 This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 15042. This T2 control element has the DNA sequence

10 CAAATCGGTAGGTAAATTGCCAAACTGAAAATTCCGGCAAATCGGCA
AATTCCCGCAACTAACATTCCGGCAAATCGGCAAATTGCTCGAACT

There are no genes controlled by this T1/T2 loop.

This long T1/T2 double stranded DNA loop modulates the expression of the
15 following C1/C2 short loops

A C1/C2 short loop on chromosome 3 whose identifier is 14841 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

20 AAAAATTCGGCAAGTCGGAATTTCCGAAAATGAAAATTCCGGCAA
ATCGGCAAATTGCCCGAATTGAAAATTCCCTGGCAAATCAGCAAATTGCG
GCAAATCGGCAATTGCCGAAAATGAAAATTCCGGCAAAT

25 This T1-T2 loop also modulates the C1/C2 short loops numbered 14842 to 15040

A C1/C2 short loop on chromosome 3 whose identifier is 15041 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

30 CGGCAATTGCCGTGGCAATTGCCAATTGCCGAAATTTCATTCCG
GCAA

The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

5 A C1/C2 short loop on chromosome 4 whose identifier is 16760 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene T23E1.2 and has the DNA sequence

10 GGCAAATTGCCGAAATTGAACATTCCGGCAAATCGGCAAATTGCCGGAA
TTAACATTCCGGCAAATCGGCAAATTGCCGGATTGAACATTCCGGC
AAATCGGCAAATTGCCGGATTGA

The match between the T1 sequence and the C1/C2 sequence is

15 ATTTCCGGCAAATCGGCAAATTGCCGGATTGAA

The match between the T2 sequence and the C1/C2 sequence is

TGAACATTCCGGCAAATCGGCAAATTGC

20

25 A double stranded DNA loop of length 98.488 kilo-bases on chromosome 3 is bounded on the left by a T1 sequence whose identifier is 15365. This T1 control element has the DNA sequence

30 AAAATTCCGGCAAATCGGCAATTGCCAAAAATTGAAATTCCGGCAA
TCGGCAATTGTCAAAAATGAAAATTCCGGCAAATCGGCAAATTGCCGA
AAATGAAAATTCCGGCAAATCGGCAAATTCCGGAACTGAAAATTCCG
GCAAATCGGCAATTGCCATAAATGAACATTCCGG...GGCGAAAATTAAA
ATTCCGCCATATCGGCAATTGCCAAAAATTAAAATTCCGGCAAATC

GGCAAATTGCCGGAATTCAAAATTCCGGCAAACCGGCAAATTGCCGGA
CTCAAAATTCCCGGCAAATCAGCAAATTGCCGGAATT

5 This double stranded DNA loop is bounded on the right by a T2 control element whose identifier is 15627. This T2 control element has the DNA sequence

TGGCAAACCGGCAAATTGCCGGAATTGAACATTCCGGCAAATCGGCAAT
TTGCCGGAATTGAAATT

10 There are no genes controlled by this T1/T2 loop.

This long T1/T2 double stranded DNA loop modulates the expression of the following C1/C2 short loops

15 A C1/C2 short loop on chromosome 3 whose identifier is 15366 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

20 TGCCGATTGCCGAAATTTCATTTCGGCAATTGCCGATTGCCGAA
ATTTCATT

This T1-T2 loop also modulates the C1/C2 short loops numbered 15366 to 15624

25 A C1/C2 short loop on chromosome 3 whose identifier is 15625 controls the expression of the genes of one or more other T1/T2 long loops. This C1/C2 short loop has the DNA sequence

TCAAGCAAATTGTCAAATCGCGGAACTAACATTCGGCAAATCGGCA
AATT

30 The expression of genes in this T1/T2 long loop is controlled by the following C1/C2 short loops.

A C1/C2 short loop on chromosome 4 whose identifier is 16760 controls the expression of the genes in this T1/T2 long loop. This C1/C2 short loop is expressed as a RNA single strand that is 3'UTR to the gene T23E1.2 and has the DNA sequence

5

GGCAAATTGCCGAAATTGAACATTCCGGCAAATCGGCAAATTGCCGGAA
TTGAACATTCCGGCAAATCGGCAAATTGCCGGATTGAACATTCCGGC
AAATCGGCAAATTGCCGGATTGA

10 The match between the T1 sequence and the C1/C2 sequence is

ATTCCGGCAAATCGGCAAATTGCCGGATT

The match between the T2 sequence and the C1/C2 sequence is

15

CGGCAAATTGCCGGATTGAACATTCCGGCAAATCGGCAA

Claims

What is claimed is:

1. A method of identifying DNA sequences that control the expression of different collections of genes in a genome comprising, detecting selected DNA sequences adjacent to some genes excluding exons and introns.
2. A method of identifying DNA sequences that control the expression of different collections of genes comprising, detecting, by computer, one or more pairs of non-adjacent DNA sequences to which are bound to two RNA sequences.
3. A method of identifying DNA sequences that control the expression of different collections of genes in a genome comprising detecting changes in connectron behavior in the genome.
4. A method of modifying the expression of different gene collections in a genome, comprising detecting changes in connectron behavior as a result of an exogenous stimulus.
5. A method of detecting where and when new genes are being integrated into a host genome comprising detecting the connectrons in said host genome.
6. A method of detecting the expression effect of different gene collections in a given body comprising detecting the back and forth flow of connectrons between the chromosomes thereof.
7. A method of modifying a given body comprising modifying the connectron organization therein.

8. A method of detecting connectron control and target sequences in a given genome comprising:

determining the base composition of said genome,
determining one or more sites of control sequence organization, and/or
determining one or more sites of target application.

9. A method of determining the response of a cell in any tissue to changes in the cell's environment and/or genetic composition comprising providing a complete genomic DNA sequence for the organism and determining the effect of changes in connectrons due to application of a given exogenous stimulus to the genome.

10. In prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, the tetradic relationship T1=C1 and T2=C2 where T1 and T2 are DNA sequences 20 or more bases in length, where the C1 sequence is adjacent to the C2 sequence, where the T1 and T2 sequences are on the same chromosome, and where the C1/C2 sequences are on the same chromosome as T1 and T2 or where the C1/C2 sequences are on a chromosome different from T1 and T2, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

11. In prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, the connectron relationship that permits many different C1/C2 short loops to control the existence of a T1-T2 long loop and wherein said C1/C2 short loops can be on the same chromosome or on different chromosomes from the T1-T2 long loop, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 540 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

12. In prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, the connectron relationship that permits one C1/C2 short loop to control the existence of many T1-T2 long loops, the C1/C2 short loop can be on the same chromosome or on different chromosomes from the T1-T2 long loops, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

13. The connectron relationships between prokaryotes and their plasmids wherein said connectrons implement a control mechanism between the two genomes that makes it possible from them to form a symbiotic relationship, and in the case of *D. radiodurans* the relationship is not symmetric, and the *D. radiodurans* genome sends C1/C2 short loops to the MP1 plasmid, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

14. The connectron relationships that exist in plant and higher animals.
15. In prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, the connectron relationship that permits one C1/C2 short loop to control the existence of one or more T1-T2 long loops without being subject to any expression controls other than those of the gene to which the C1/C2 is 3'UTR, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart,

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart, and

3'UTR - untranslated 3' end of an mRNA is beyond the end of the last exon, a stop codon in the mRNA causes the ribosome to stop the translation of mRNA into protein.

16. In prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, the connectron relationship that permits one C1/C2 short loop to control the existence of one or more T1-T2 long loops such that this C1/C2 short loop is itself subject to expression control by another T1-T2 long loop which surrounds it, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

17. In prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, the connectron relationship that permits one C1/C2 short loop to control the existence of the T1-T2 long loop that surrounds it, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 50 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

18. The connectron relationship that do not have any genes within the T1-T2 long loop, wherein:

T1 sequence is any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, and the T2 or T1 sequences must be between about 1kb and 105kb apart.

19. The geneless connectron relationship where one C1/C2 short loop controls the existence of many geneless T1-T2 long loops, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

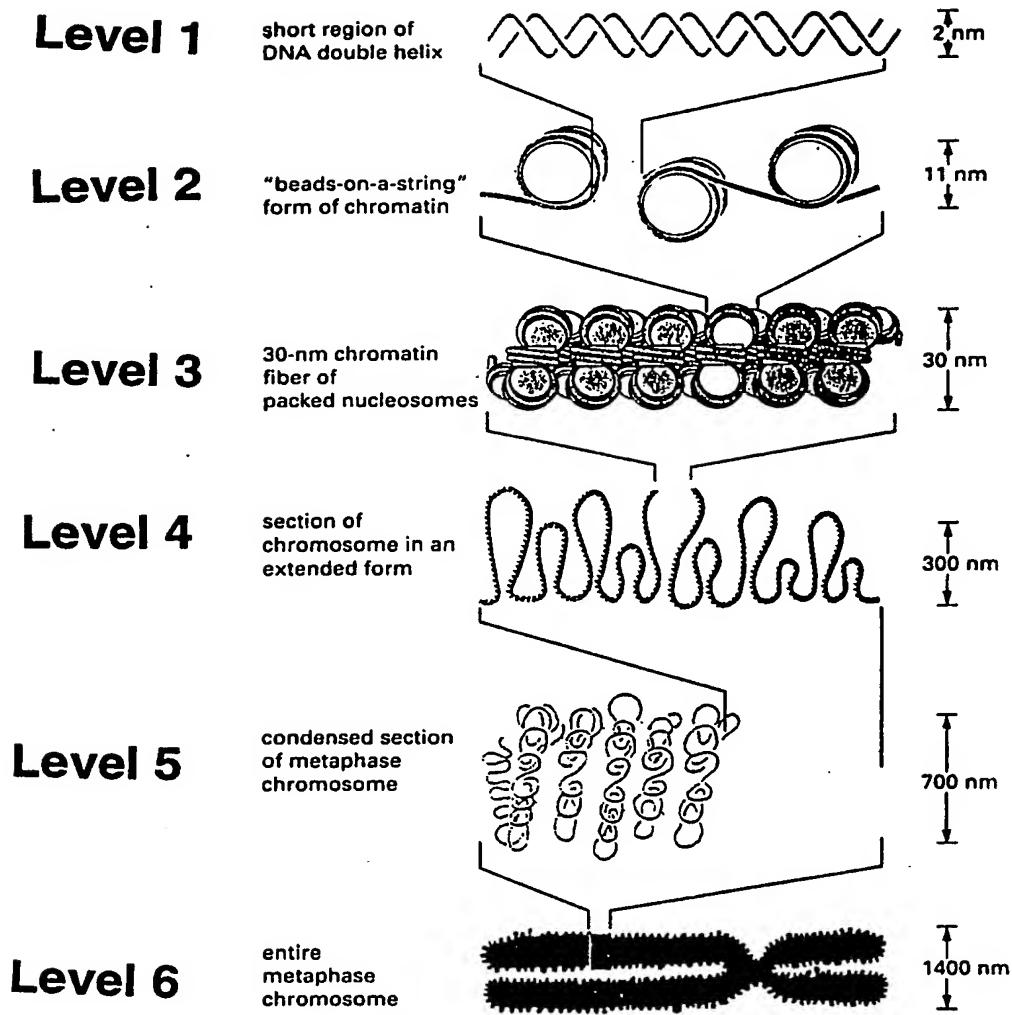
C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

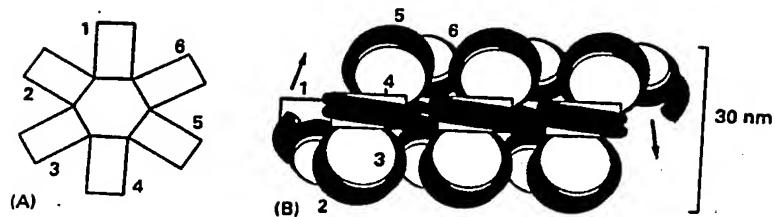
T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

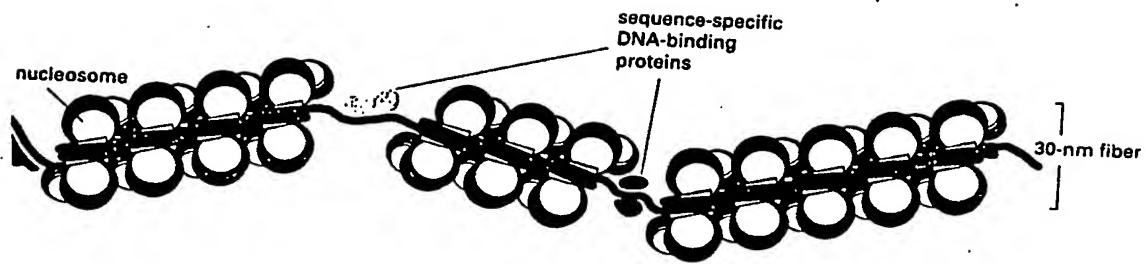
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**Figure 1**

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(a)



(b)

Figure 2

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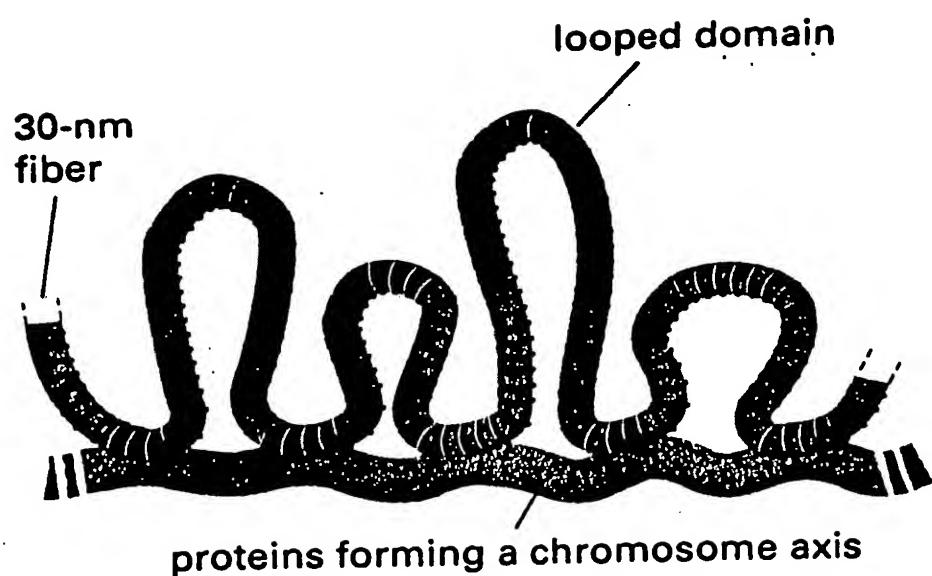
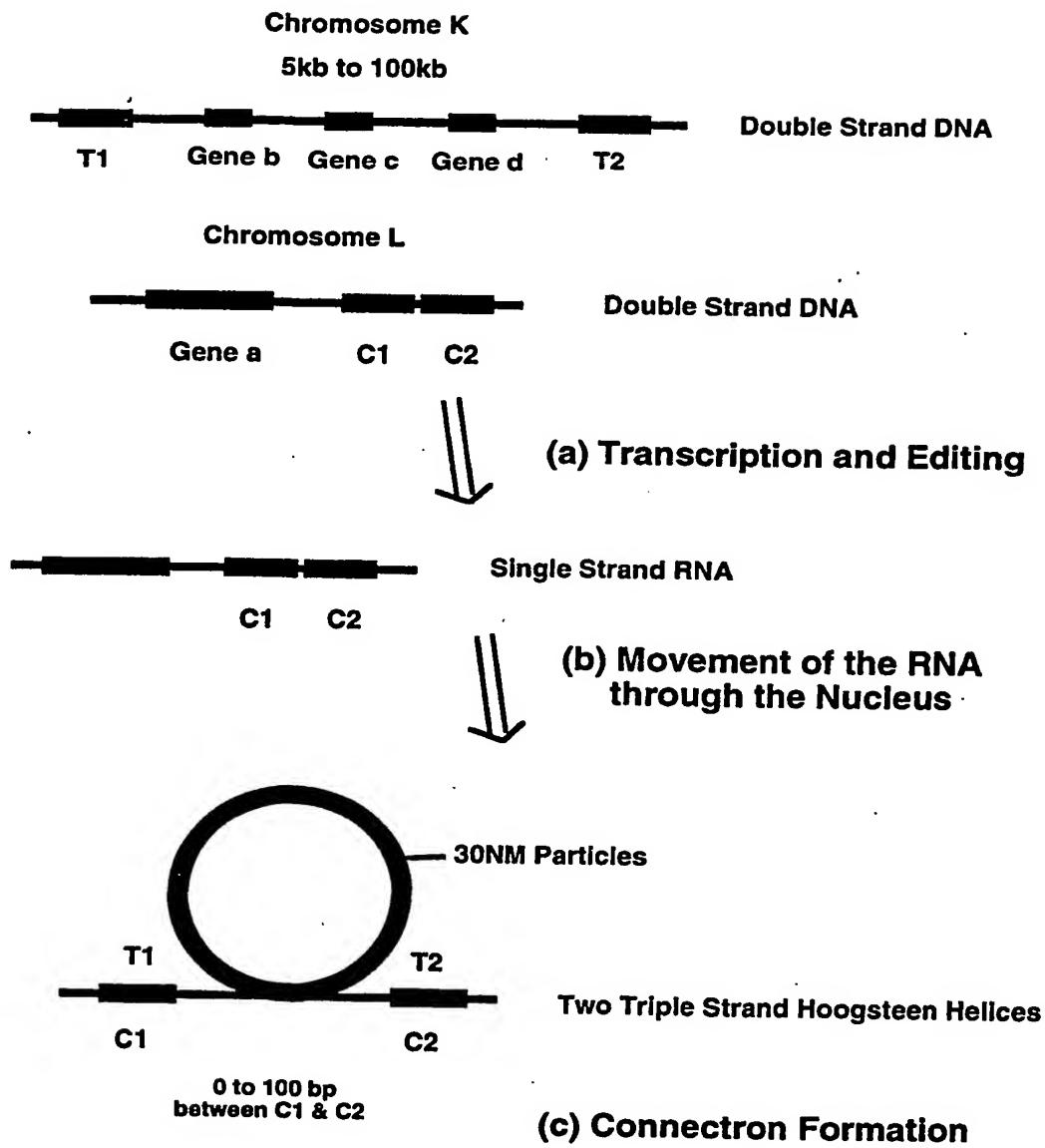


Figure 3

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**Figure 4**

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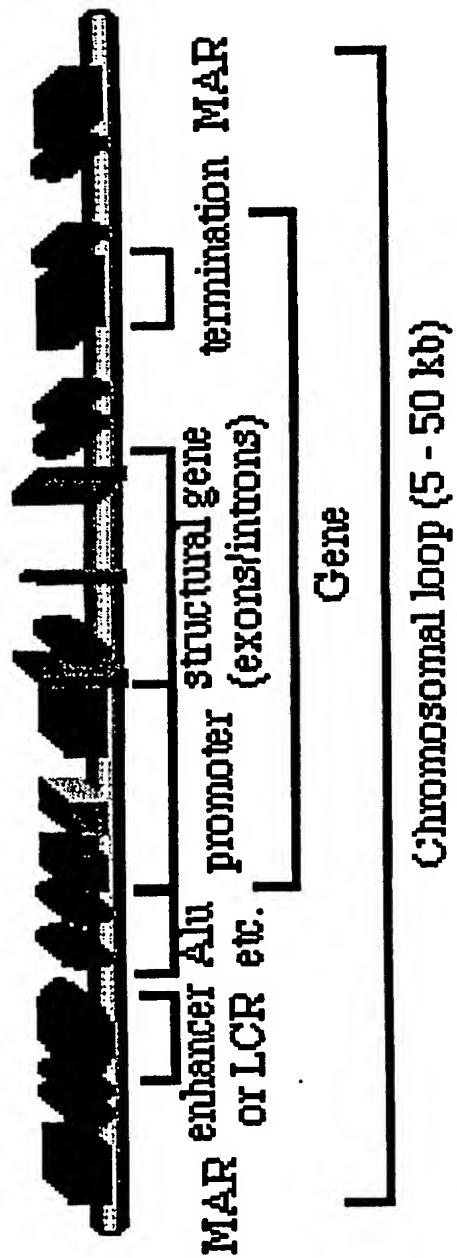


Figure 5

Chromosomal loop (5 - 50 kb)

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Genome	Chromosome Number	Number of Genes	Chromosome Length (bp)	Total Number of C1/C2 Short Loops	Total Number of T1/T2 Long Loops	C1/C2 Short Loops	T1/T2 Short Loops	Number of Unique T1/T2 Long Loops	Percent of T1/T2 Long Loops	Number of Unique Genes	Percent of Genes Contained
E. coli	I	4,289	4,639,221	544	544		214		17.8	24.78	
H. pylori	I	1,566	1,667,867	19	19		17		1.0	10.53	
M. leprae	I	1,715	1,664,970	1,648	1,648		122		36.0	35.12	
D. radiodurans	I	2,580	2,648,638	974	628	246	246		29.2		
■	III	357	412,348	113	14	17	17		1.0		
■	IV - Plasmid MP1	131	177,466	803	1,239	87	87		46.4		
■	IV - Plasmid CP1	35	45,704	91	80	28	28		4.5	77.14	
	Totals	3,103	3,284,156	1,981	1,981	378	378		81.1		
S. cerevisiae	I	110	230,209	898	283	26	26		11.2		
	II	447	813,137	1,387	2,516	568	568		1.094		
	III	172	315,339	1,314	1,762	336	336		53.3		
N	IV	845	1,520,519	4,253	3,689	1,298	1,298		1.279		
V	V	280	576,870	2,034	2,888	638	638		1.111		
VI	VI	127	270,148	438	155	153	153		45.5		
VII	VII	629	1,050,936	3,003	2,776	981	981		98.2		
VIII	VIII	279	552,638	1,207	410	433	433		1.66		
X	IX	236	439,685	248	81	113	113		48.8		
X	X	406	745,440	1,691	2,019	541	541		7.69		
X	XI	351	666,448	513	228	128	128		68.8		
XII	XII	578	1,078,173	3,010	4,282	951	951		1.821		
XIII	XIII	501	924,430	2,306	3,254	680	680		1.228		
XIV	XIV	458	784,328	1,579	490	528	528		1.44		
XV	XV	609	1,091,283	1,630	626	543	543		2.10		
XVI	XVI	510	948,056	2,628	2,680	820	820		9.67		
	Totals	6,538	12,057,849	28,139	28,139	8,737	8,737		10.697	19.88	
C. elegans	I	2,474	16,183,833	315,926	155,815	12,245	12,245		24.537		
	II	3,043	17,004,925	132,735	92,595	13,370	13,370		26.847		
	III	2,100	12,114,540	93,171	89,303	8,472	8,472		13.669		
IV	IV	2,523	15,887,371	67,196	99,552	10,641	10,641		14.420		
V	V	4,358	21,280,512	337,841	246,674	15,612	15,612		35.571		
	X	2,625	17,624,844	611,789	63,719	6,138	6,138		7.805		
	Totals	17,123	100,096,025	1,559,658	1,559,658	66,478	66,478		245,449	33.6	

Table 1 - page 1

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Genome	Chromosome Number	Number of Genes	Chromosome Length (bp)	C1/C2 Short Loops	Total Number of T1/T2 Long Loops	Number of Unique C1/C2 Short Loops		Number of Unique T1/T2 Long Loops	Percent of Genes Controlled
						T1/T2 Long Loops	C1/C2 Short Loops		
Scaffold									
<i>D. melanogaster</i>	1	1,138	10,564,115	16,200	17,916	3,268	5,015		
	2	698	4,515,897	3,293	9,317	655	2,634		
	3	633	5,077,262	3,502	3,027	1,038	556		
	4	1,075	9,080,116	129,140	127,538	1,566	5,910		
	5	1,777	15,101,630	16,800	16,463	2,565	2,093		
	6	122	1,265,848	668	237	190	110		
	7	28	536,527	476	586	208	378		
	8	615	4,861,285	10,727	10,731	603	978		
	9	317	2,692,893	2,506	759	624	214		
	10	286	2,159,491	1,436	1,049	494	369		
	11	1,822	16,346,801	8,583	8,415	2,363	1,860		
	12	143	1,363,555	151	15	64	13		
	13	3,075	24,259,494	11,273	9,274	3,133	1,608		
	14	49	705,960	1,922	1,754	606	662		
	15	91	1,361,891	3,544	4,719	907	2,721		
	16	66	509,295	101	106	42	28		
	17	1,893	13,672,780	6,770	3,286	1,929	739		
	18	61	751,204	1,451	2,521	490	1,596		
	19	35	403,964	471	1,291	212	926		
	Totals		13,924	115,229,998	218,014	21,257	28,411	5,21	
<i>A. thaliana</i>	Ia	3,221	14,221,815	22,735	20,165	3,310	4,503		
	b	3,136	14,668,883	22,202	25,016	4,043	7,324		
	i	4,036	18,647,081	153,605	75,591	10,377	19,280		
	IV	3,823	17,550,082	523,824	601,594	6,445	54,556		
	Totals		14,216	65,087,871	722,366	24,175	86,173	7,51	
<i>H. sapiens</i>	XXI	position data not available		33,667,731	> 10,000				

Table 1 - page 2

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	Chromosome of T1-T2															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1	39	57	35	57	4	5	19	2	41		38	25	7	12	12	
2	9	70	13	27	98		22	17	1	9	36	130	15		89	
3	6	54	44	39		37	5	1		5	16	23	10	6	29	
4	10	73	93	257	158	13	138	12	2	67	9	135	144	30	38	125
5	1	47	13	42	32	5	19	1	26		76	14	5	9	18	
6													46			
7	4	72	46	114	83	7	100	14	2	64	6	83	91	15	20	73
8	10	66	13	52		25	14	3	25		58	15	3	12	16	
9	2		12	14		18	9	2	1		4		2	4	8	
10	4	9	24	48	107	1	47	9	1	59	8	38	100	10	8	81
11		27	15	39	1		15			26	5	6	29	1	11	14
12	10	68	61	107	90	8	77	2		56	2	193	73	19	25	76
13	4	78	60	134	85	2	68	8	3	71	14	60	173	10	28	127
14		66	13	56	14		16			25		15	18	4	12	28
15	3	10	20	31	79	1	27	11	1	8	8	52	78	6	7	82
16	6	54	68	126	121	9	86	14	1	51	15	100	130	20	24	137

Table 2

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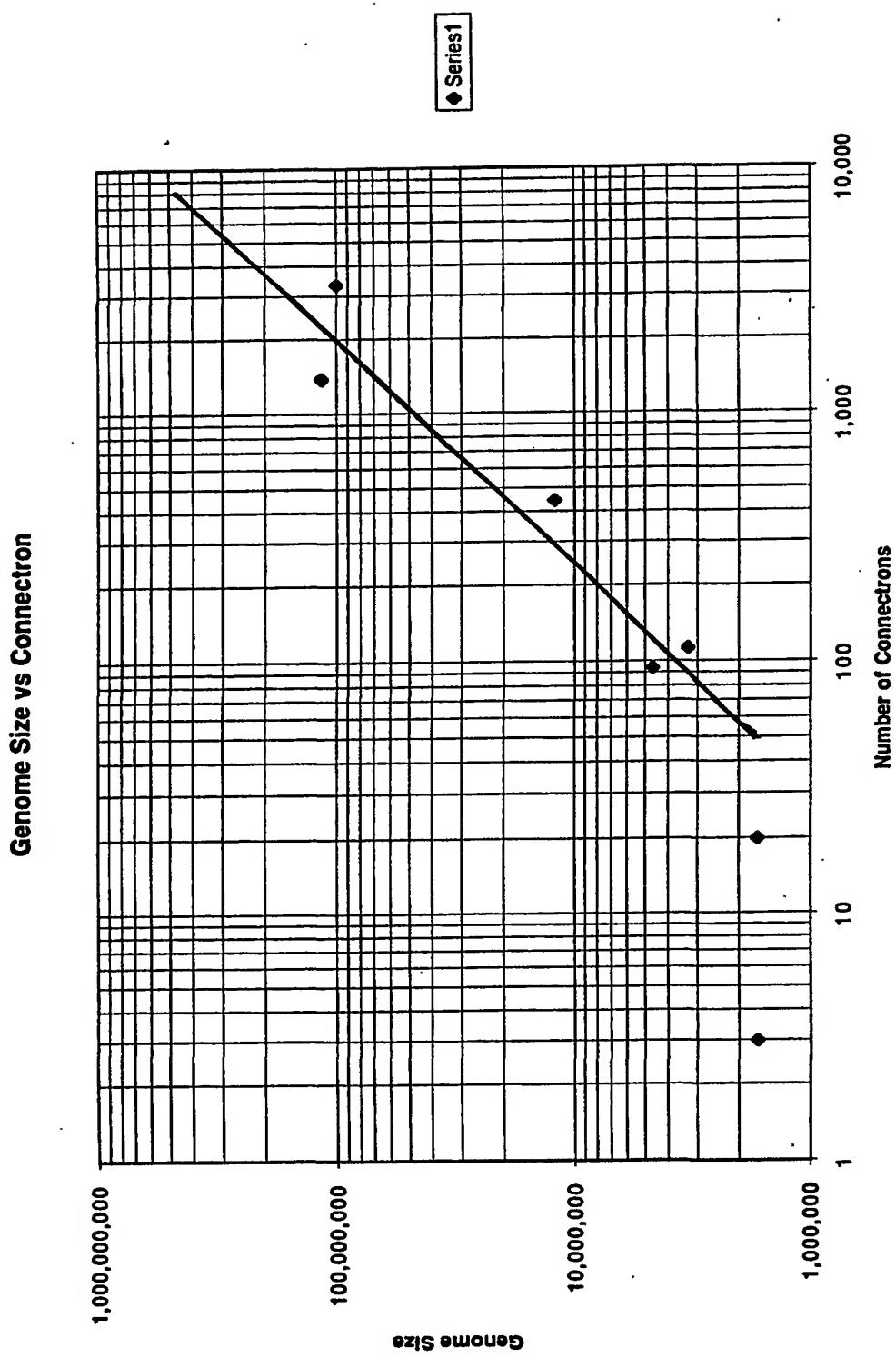


Figure 6

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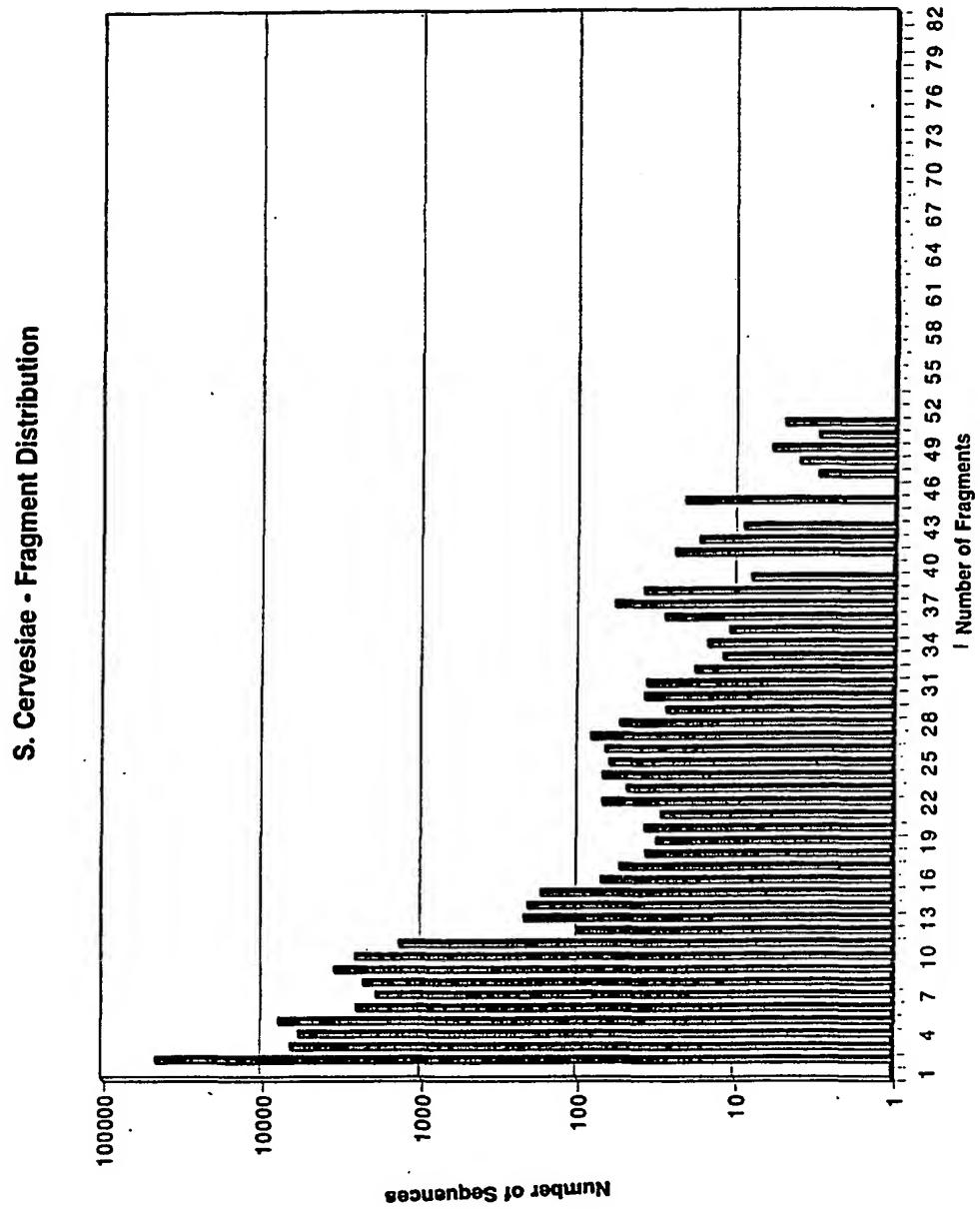


Figure 7

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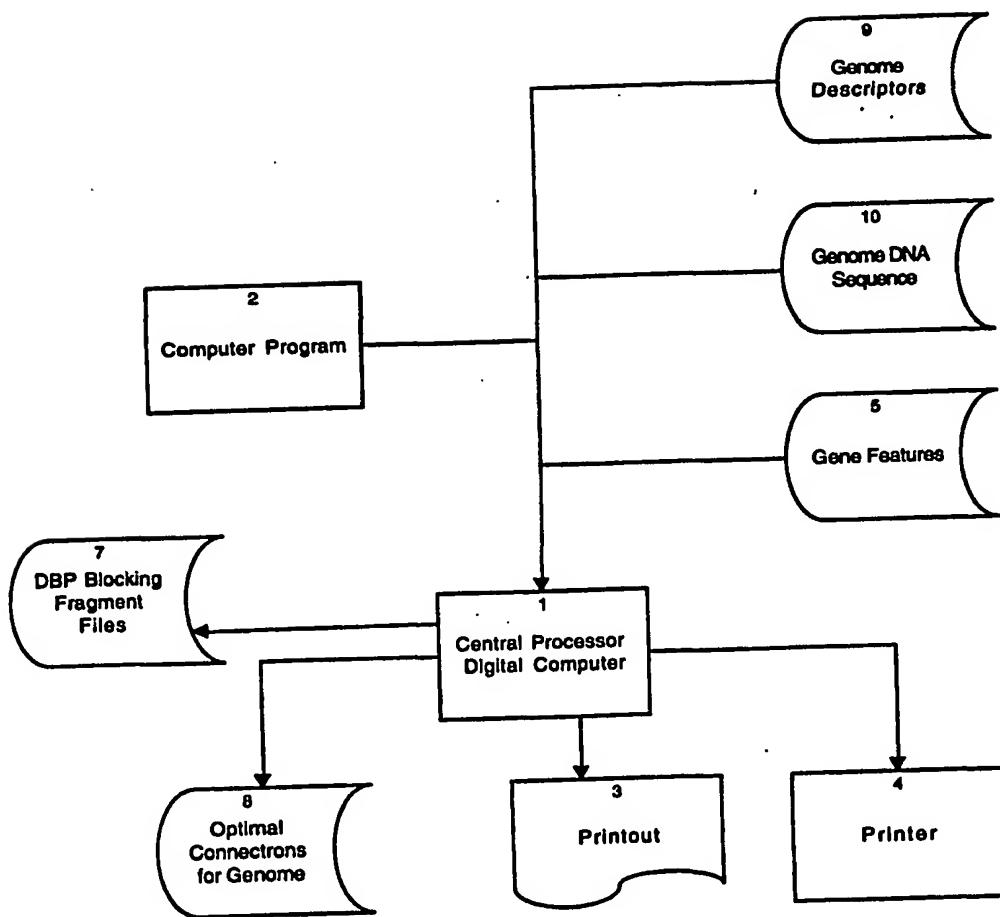
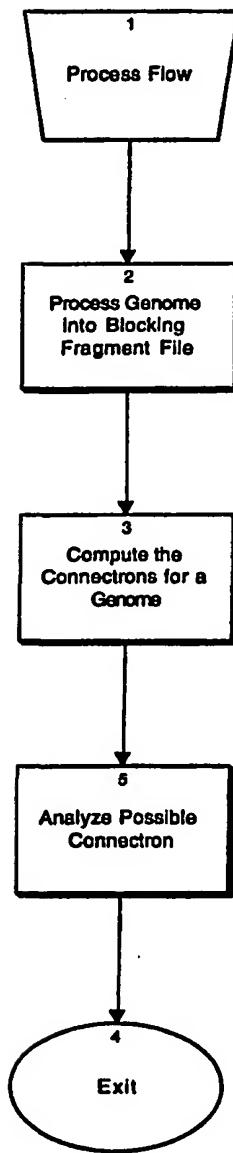


Figure 8

12/26**Figure 9**

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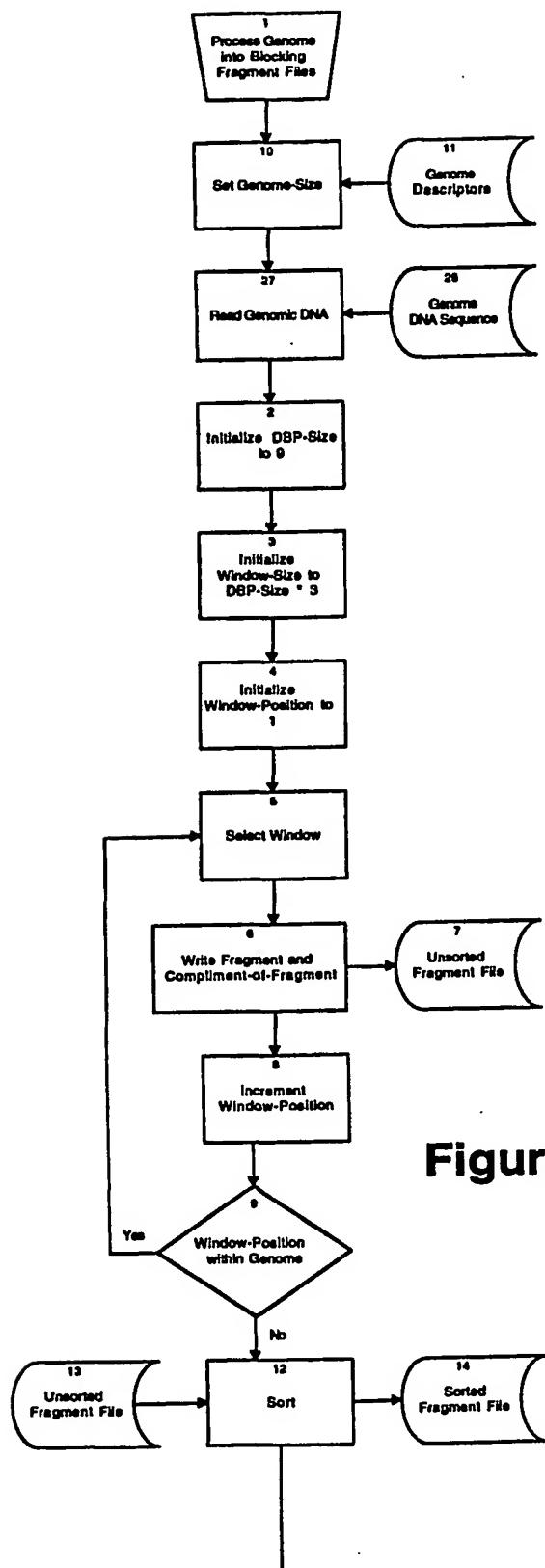


Figure 10 - page 1

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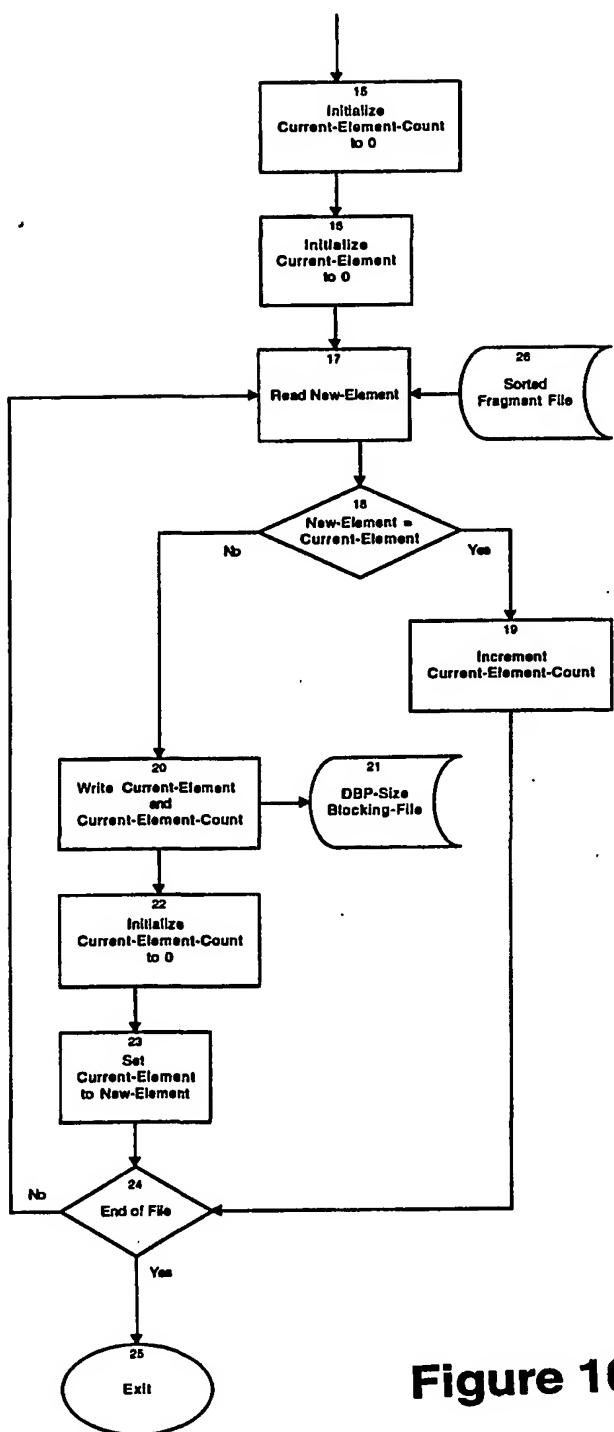
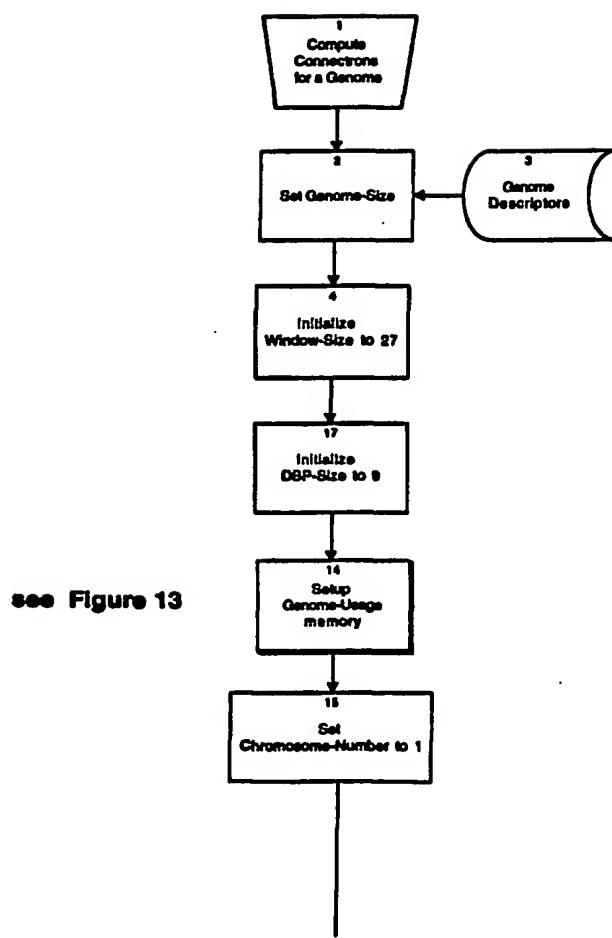


Figure 10 - page 2

15/26**Figure 11 - page 1**

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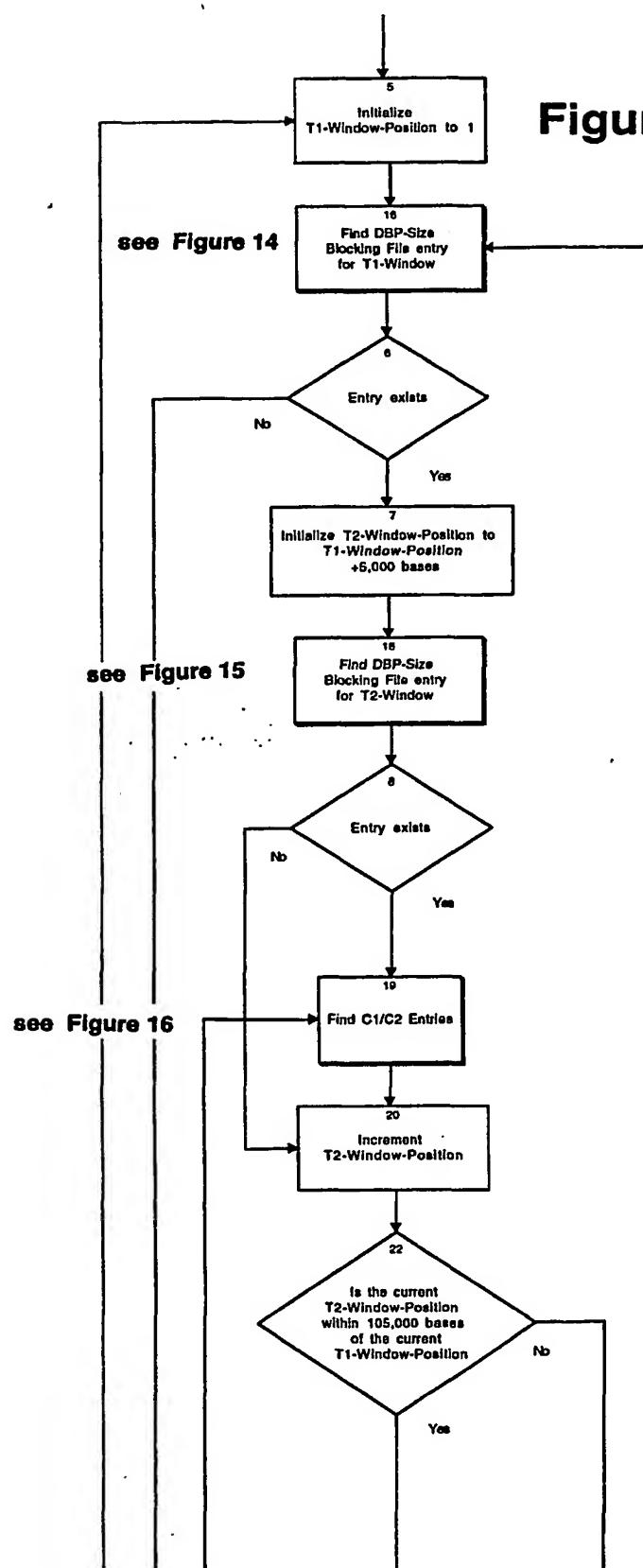
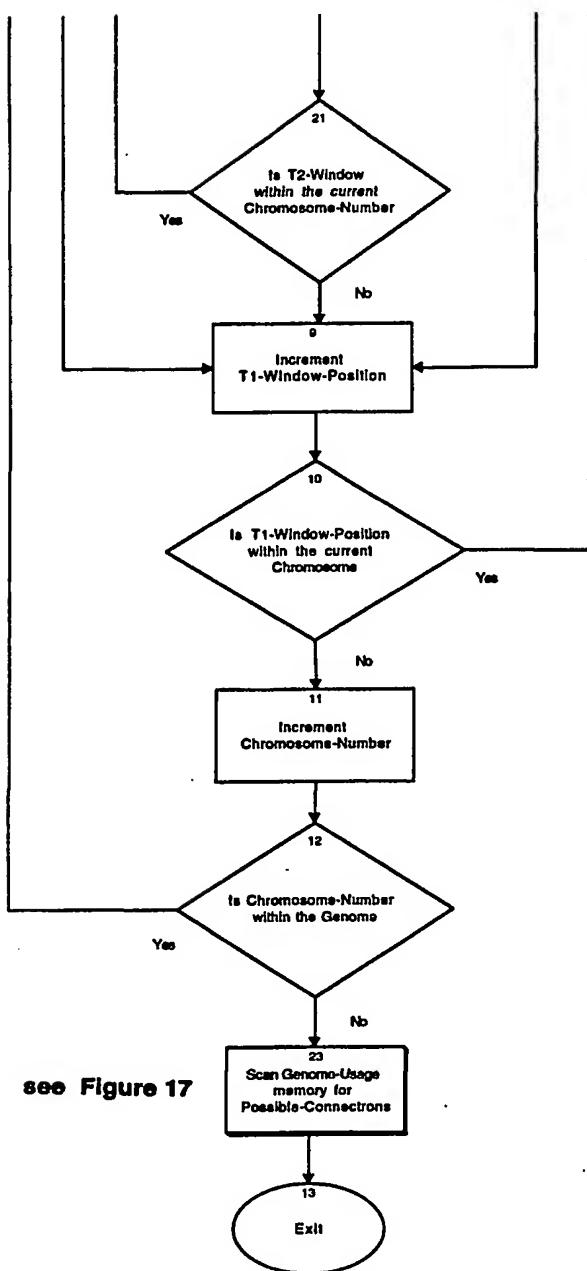


Figure 11 - page 2

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see Figure 17

Figure 11 - page 3

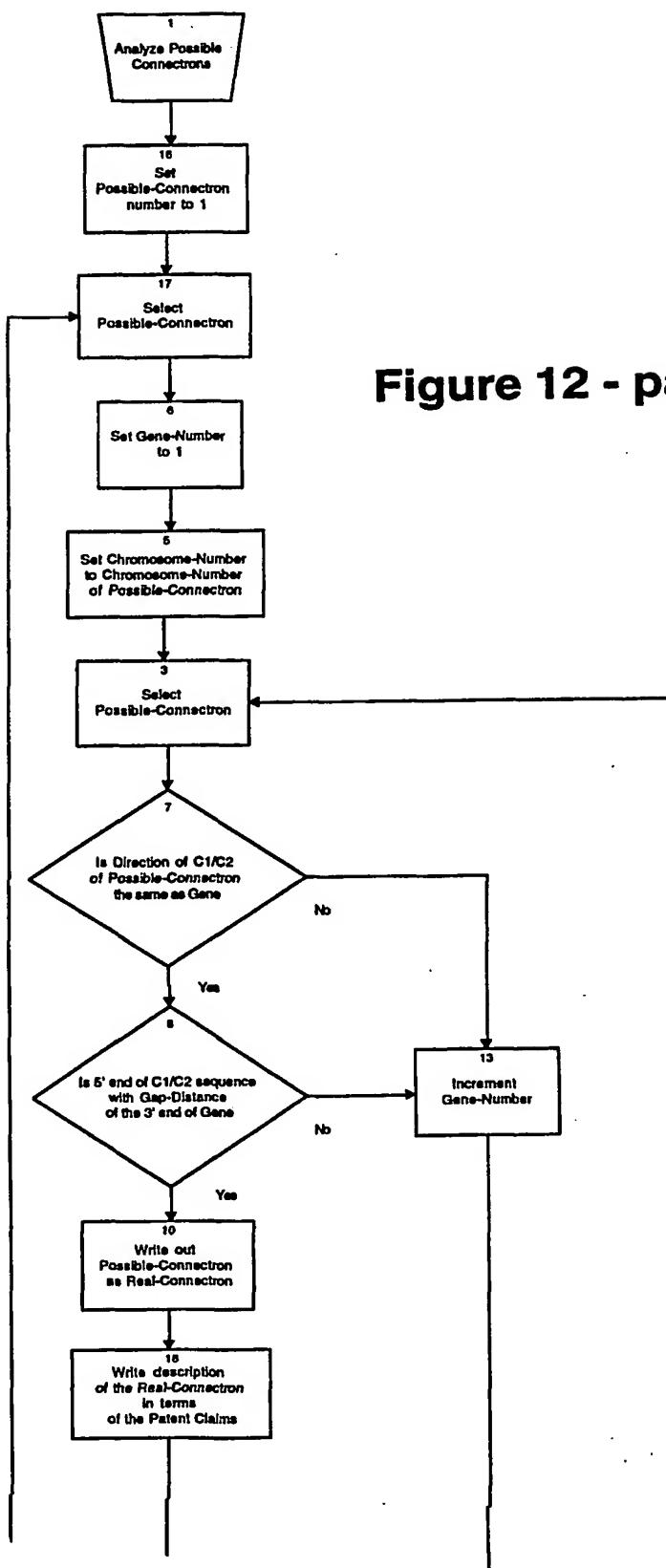
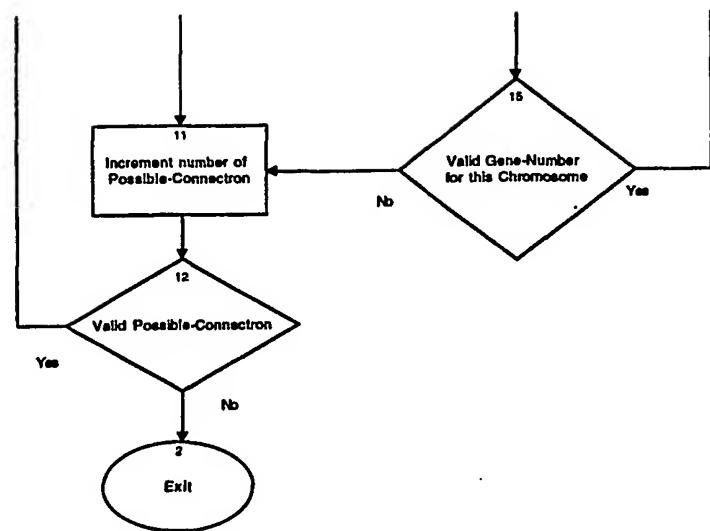


Figure 12 - page 1

19/26**Figure 12 - page 2**

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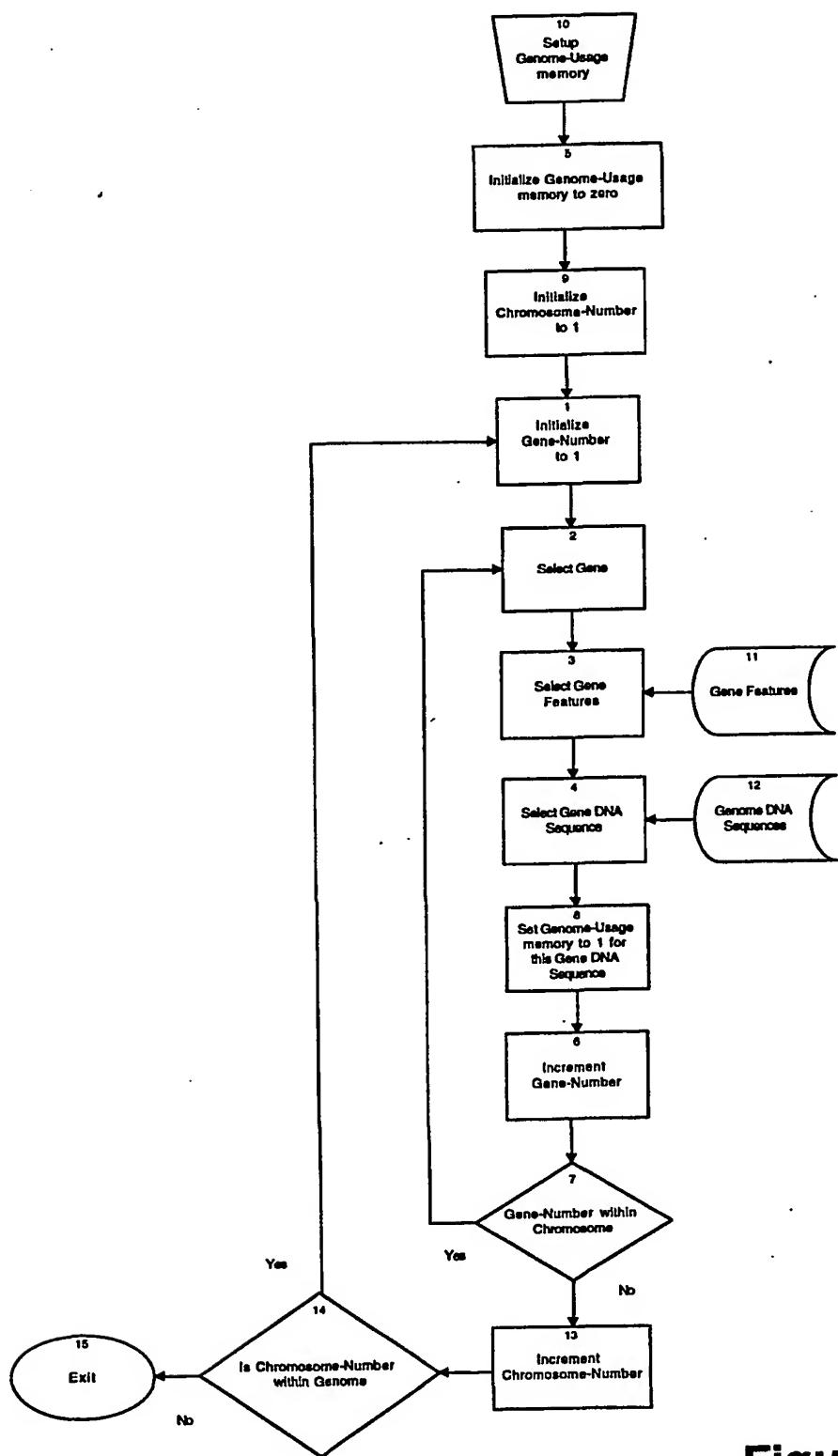
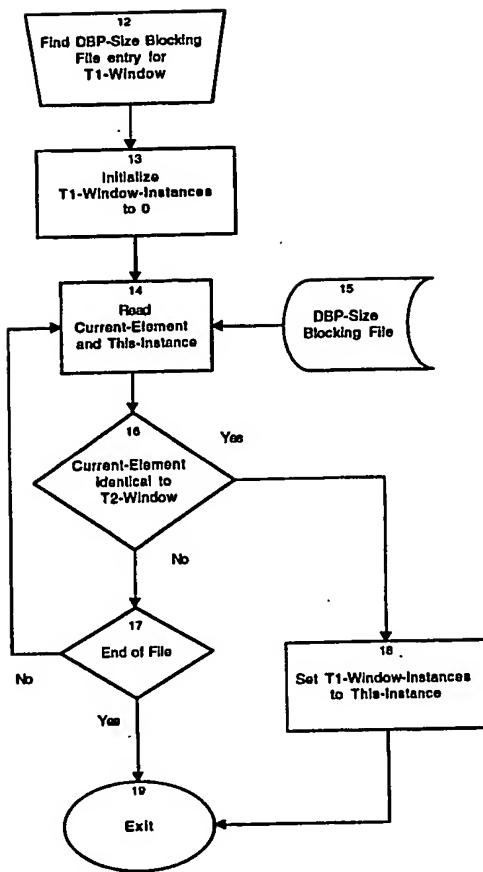


Figure 13

21/26**Figure 14**

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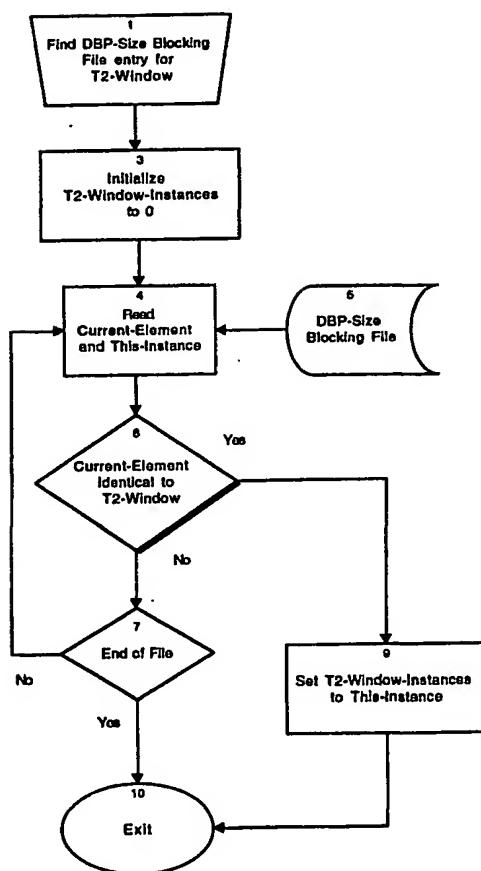


Figure 15

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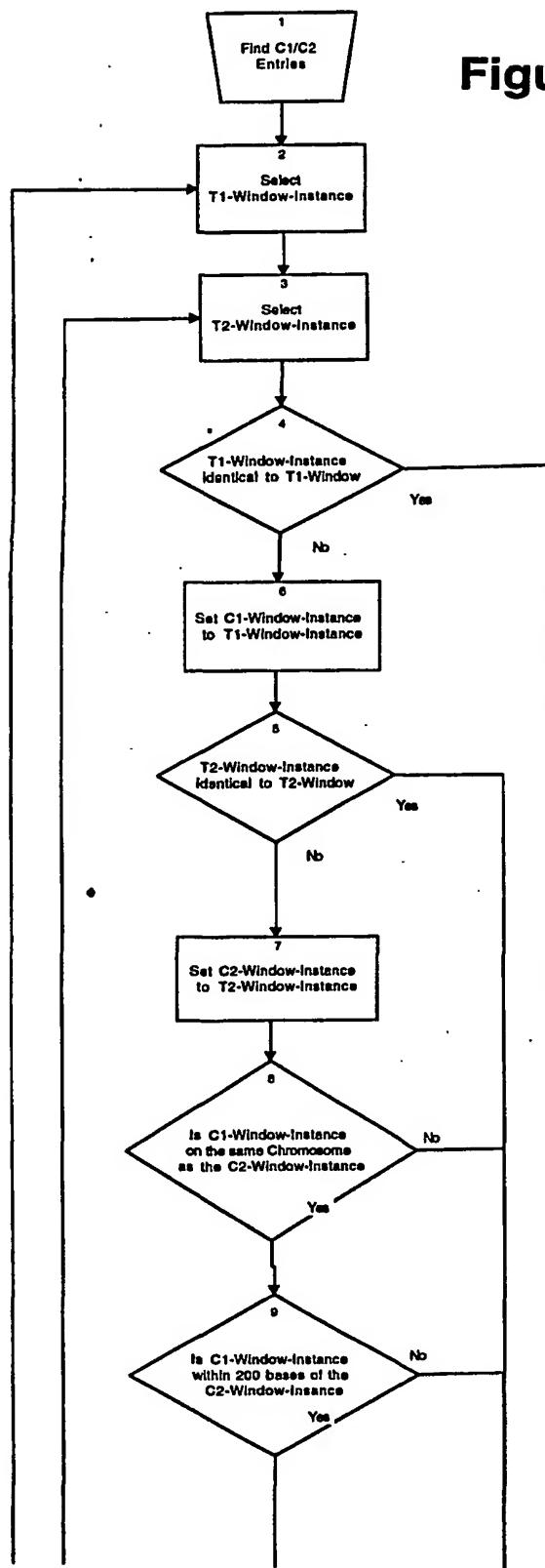


Figure 16 - page 1

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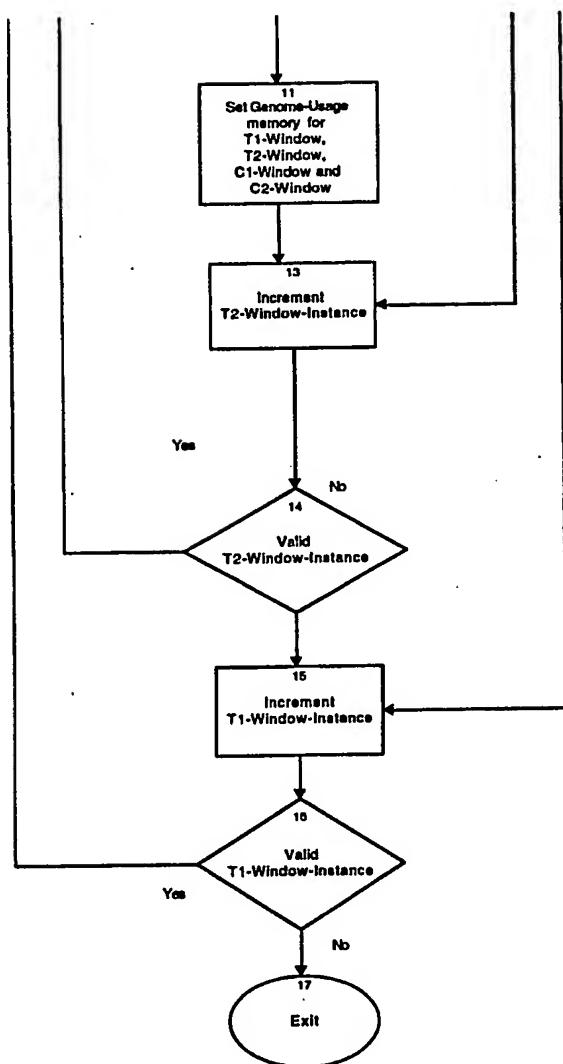


Figure 16 - page 2

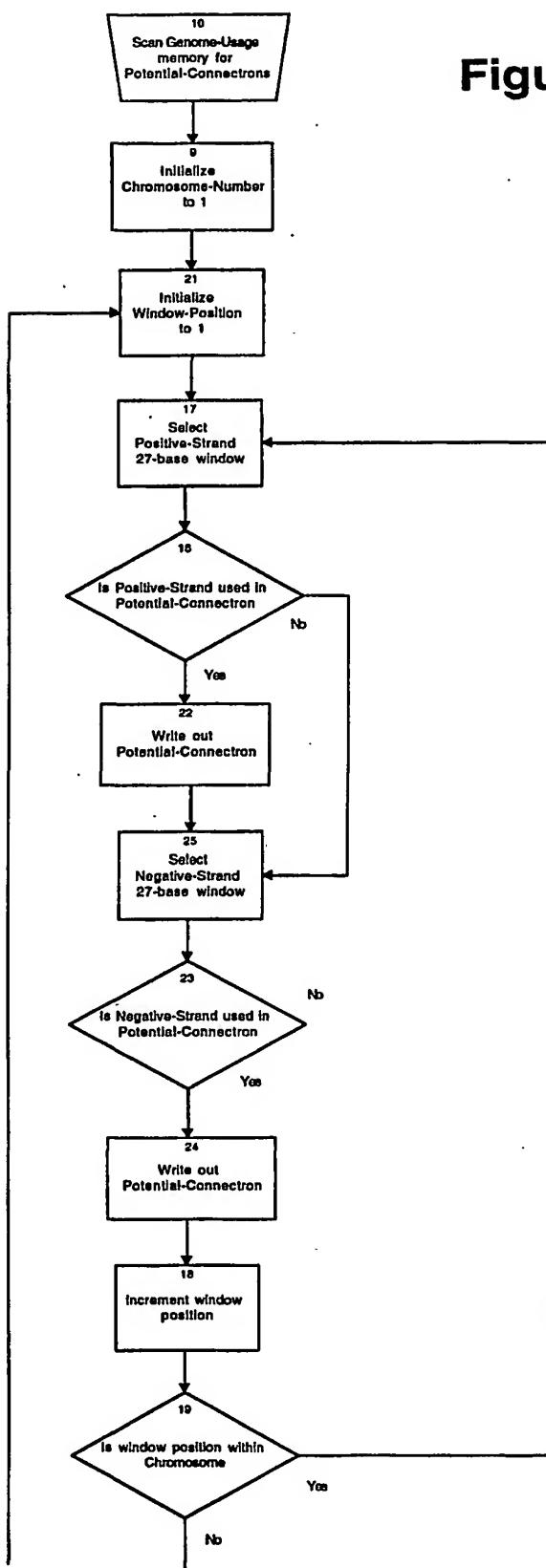


Figure 17 - page 1

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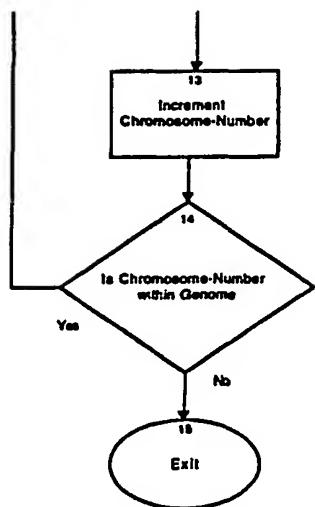


Figure 17 - page 2

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(74) Agent: ZEGEER, Jim; 801 North Pitt Street #108, Alexandria, VA 22314 (US).

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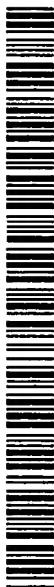
(71) Applicant: GLOBAL DETERMINANTS, INC.
[US/US]; 17800 Mill Creek Drive, Derwood, MD
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(72) Inventor: FELDMANN, Richard, J.; 17800 Mill Creek
Drive, Derwood, MD 20855-1019 (US).

Published:
— with international search report

(88) Date of publication of the international search report:
18 April 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



WO 01/94542 A3

(54) Title: ALGORITHMIC DETERMINATION OF CONNECTRONS

(57) Abstract: An algorithm has been developed to identify four DNA sequences of 20 bases or more that form a structure called a connectron. Two sequences C1 and C2 are expressed as RNA in the 3'UTR of some genes in many prokaryotic, archaea and eukaryotic genomes. The other half of a connectron is two DNA sequences T1 and T2 that are 1kb to 105kb apart on the same chromosome. The C1 sequence is identical to the T1 sequence and the C2 sequence is identical to the T2 sequence. C1/C2 and T1-T2 can be on different chromosomes. The C1/C2 RNA sequence of the gene transcript forms a triple-stranded Hoogsteen helix with the double-stranded T1 and T2 DNA sequences. The formation of connectrons blocks expression of genes between T1 and T2.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/16471

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G06F 19/00
US CL : 702/19

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 702/19

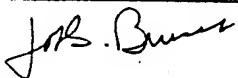
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KAIN et al. in Current Protocols in Molecular Biology. Ausubel et al. Eds. New York:John Wiley and Sons. 1996, pages 9.6.1 to 9.6.12, especially page 9.6.3.	1
X	ZHANG et al. Identification of Human Gene core Promoters in Silico. Genome Research. 1998, Vol. 8, pages 319-326, especially page 319.	2
A	Matzke et al. How and Why Do Plants Inactivate Homologous (Trans)genes? Plant Physiology. 1995, Vol. 107, pages 679-685, especially page 681.	3-18
A	Fire et al. Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans. Nature. 19 February 1998, Vol. 391, pages 806-811, especially pages 806-807.	3-18

<input type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input type="checkbox"/>	See patent family annex.
*	Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier application or patent published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 15 August 2001 (15.08.2001)	Date of mailing of the international search report 23 JAN 2002
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer John S. Brusca, Ph.D. Telephone No. (703) 308-0196 

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/16471

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest



The additional search fees were accompanied by the applicant's protest.



No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/16471

Continuation of Item 4 of the first sheet:

The title does not comply with PCT Rule 4.3 because it is longer than 7 words. The new title is as follows:

Algorithmic determination of connectrons.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1, drawn to a promoter detection comprising exclusion of introns and exons.

Group II, claim(s) 2, drawn to a promoter detection method comprising detection of DNA linked to RNA.

Group III, claim(s) 3, drawn to a promoter detection method comprising detection of connectron behavior.

Group IV, claim(s) 4, drawn to a method of modifying expression comprising detection of changes in connectron behavior.

Group V, claim(s) 5, drawn to a method of detecting integration by detection of connectrons.

Group VI, claim(s) 6, drawn to a method of detecting expression of genes by detecting flow of connectrons.

Group VII, claim(s) 7, drawn to a method of modifying a body by modification of connectrons.

Group VIII, claim(s) 8, drawn to a method of detection of connectrons by any of three methods:a) determining base composition, b) determining one or more sites of control sequence organization, and c) determining sites of target application.

Group IX, claim(s) 9, drawn to a method of determining cell response by use of complete genome sequences and detection of changes in connectrons caused by stimulus to the genome.

Group X, claim(s) 10, drawn to polynucleotides with a defined symmetry.

Group XI, claim(s) 11, drawn to polynucleotides with a first connectron relationship.

Group XII, claim(s) 12, drawn to polynucleotides with a second connectron relationship.

Group XIII, claim(s) 13, drawn to polynucleotides with a third connectron relationship.

Group XIV, claim(s) 14, drawn to polynucleotides with a fourth connectron relationship of plants and higher animals.

Group XV, claim(s) 15, drawn to polynucleotides with a fifth connectron relationship.

Group XVI, claim(s) 16, drawn to polynucleotides with a sixth connectron relationship.

Group XVII, claim(s) 17, drawn to polynucleotides with a seventh connectron relationship.

Group XVIII, claim(s) 18, drawn to polynucleotides with an eighth connectron relationship.

Group XIX, claim(s) 19, drawn to polynucleotides with a ninth connectron relationship.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

Group VIII is drawn to three species of detection of connectrons comprising the alternative steps of: 1) determining base composition, 2) determining one or more sites of control sequence organization, and 3) determining sites of target application.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/16471

The claims are deemed to correspond to the species listed above in the following manner:

The following claim(s) are generic: 8.

The inventions listed as Groups 1-19 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: PCT Rule 13.1 and Annex B do not provide for unity of invention between two or more different products or methods of use that share a special technical feature. To the extent the groups have a special technical feature of a connectron, the groups are drawn to different methods of use or detection of connectrons. To the extent the groups are drawn to compositions of connectrons, the groups are drawn to compositions with different structures that lack a common special technical feature.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The species listed for Group VIII are drawn to three different methods with different steps that produce different results.

Continuation of B. FIELDS SEARCHED Item 3:
Medline, Biosis, US Patent, Derwent World Patent Index
search terms:promoter, software, connectron